STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 169035

TO: Cybille Delacroix
Location: rem/3A78/3C70
Art Unit: 1614
Thursday, October 20, 2005

Case Serial Number: 10/634641

From: Paul Schulwitz
Location: Biotech-Chem Library
REM-1A65
Phone: 571-272-2527

Paul.schulwitz@uspto.gov

Search Notes

Examiner Delacroix,

Please review the attached search results.
If you have any questions or if you would like to refine the search query, please feel free to contact me at any time.

Thank you for using STIC search services!

Paul Schulwitz
Technical Information Specialist
REM-1A65
571-272-2527

Access DB# 167055

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: C. Delacroix Examiner #: 71100 Date: 10-19-05

Art Unit: 1614 Phone Number 30 2-0572 Serial Number: 10/634,641

Mail Box and Bldg/Room Location: 3C70 3A78 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need. MG

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of invention: _____

Inventors (please provide full names): please see BIB sheet attached

Earliest Priority Filing Date: _____

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search the method of claim 11. Key terms are highlighted.

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OCT 20 2005
TECH/CHEM. DIVISION
(STIC)

Please rush
Thanks
CM

Rush Search Approved Christopher Low 19 Oct 2005

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable
Searcher:	NA Sequence (#)		STN
Searcher Phone #:	AA Sequence (#)		Dialog
Searcher Location:	Structure (#)		Questel/Orbit
Date Searcher Picked Up:	Bibliographic		Dr.Link
Date Completed:	Litigation		Lexis/Nexis
Searcher Prep & Review Time:	Fulltext		Sequence Systems
Clerical Prep Time:	Patent Family		WWW/Internet
Online Time:	Other		Other (specify)

ETO-1590 (8-01)

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BIBDATASHEET

CONFIRMATION NO. 7194

Bib Data Sheet

SERIAL NUMBER	FILING DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
10/634,641	08/04/2003 RULE	514	1614	TECH-004

APPLICANTS

Kyoya Takahata, Okayama-shi, JAPAN;

** CONTINUING DATA **********

** FOREIGN APPLICATIONS **********
JAPAN 2002-353649 12/05/2002

IF REQUIRED, FOREIGN FILING LICENSE GRANTED
** 11/01/2003

Foreign Priority claimed	STATE OR COUNTRY	SHEETS DRAWING	TOTAL CLAIMS	INDEPENDENT CLAIMS
☑ yes ☐ no 35 USC 119 (a-d) conditions met ☑ yes ☐ no ☐ Met after Allowance Verified and Acknowledged Examiner's Signature Initials	JAPAN	6	14	4

ADDRESS
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1900 UNIVERSITY AVE
SUITE 200
EAST PALO ALTO , CA
94303

TITLE
Anti-tumor pharmaceutical composition comprising N-vanillyl fatty acid amide

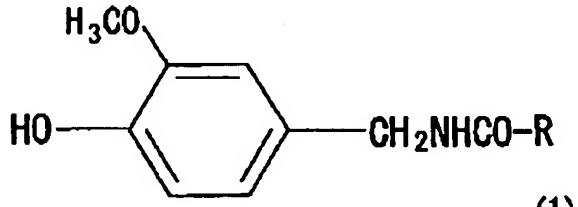
FILING FEE RECEIVED 1312	FEES: Authority has been given in Paper No. _____ to charge/credit DEPOSIT ACCOUNT No. _____ for following:	☐ All Fees ☐ 1.16 Fees (Filing) ☐ 1.17 Fees (Processing Ext. of time) ☐ 1.18 Fees (Issue)

Atty Dkt. No.: ORJN-004
USSN: 10/634,641

AMENDMENTS TO THE CLAIMS:

1. - 10. **(Canceled)**

11. **(Previously Presented)** A method for the treatment of melanoma or leukemia comprising administering to a patient in need thereof an effective amount of a N-vanillyl fatty acid amide of formula (1):



(1)

wherein -CO-R group represents a saturated or unsaturated fatty acid residue containing from 14 to 32 carbon atoms.

12. -14. **(Canceled)**

15. **(Previously Presented)** The method of claim 11, wherein the -CO-R group is a member selected from the group consisting of saturated fatty acid residues containing from 14 to 32 carbon atoms.

16. **(Previously Presented)** The method of claim 15, wherein the -CO-R group is a member selected from the group consisting of myristic acid residue (C14), palmitic acid residue (C16) and stearic acid residue (C18).

17. **(Previously Presented)** The method of claim 11, wherein the -CO-R group is a member selected from the group consisting of unsaturated fatty acid residues containing from 14 to 32 carbon atoms.

18. **(Previously Presented)** The method of claim 17, wherein the -CO-R group is a member selected from the group consisting of unsaturated fatty acid residues having from 1 to 3 double bonds and containing 18 carbon atoms and unsaturated fatty acid residues having 4 or 5 double bonds and containing 20 carbon atoms.

19. **(Previously Presented)** The method of claim 18, wherein the -CO-R group is a member selected from the group consisting of oleic acid residue (C18:1), ricinoleic acid residue (C18:1), linoleic acid residue (C18:2), linolenic acid residue (C18:3) and eleostearic acid residue (C18:3).

20. **(Previously Presented)** The method of claim 18, wherein the -CO-R group is a member selected from the group consisting of arachidonic acid residue (C20:4) and eicosapentaenoic acid residue (C20:5).

21. **(Previously Presented)** The method of claim 17, wherein the -CO-R group is a member selected from the group consisting of unsaturated fatty acid residues having four or more double bonds and containing 22, 24, 26, 28 or 32 carbon atoms.

22. **(Previously Presented)** The method of claim 21, wherein the -CO-R group is 4,7,10,13,16,19-docosahexaenoic acid residue (C22:6).

INVENTORS

L42 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:470289 HCAPLUS
DOCUMENT NUMBER: 141:17594
TITLE: Antitumor pharmaceutical composition comprising N-**vanillyl fatty acid** amide
INVENTOR(S): **Takahata, Kyoya**
PATENT ASSIGNEE(S): Kureha Chemical Industry Company, Limited, Japan
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1426047	A1	20040609	EP 2003-254668	20030725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2004182674	A2	20040702	JP 2002-353649	20021205
US 2004110844	A1	20040610	US 2003-634641	20030804
PRIORITY APPLN. INFO.:			JP 2002-353649 A	20021205

OTHER SOURCE(S): MARPAT 141:17594
AB The present invention provides an antitumor pharmaceutical composition comprising a N-**vanillyl fatty acid** amide containing a saturated or unsatd. **fatty acid** residue containing 14 to 32 carbon atoms which is related to capsaicin. An antitumor pharmaceutical composition comprising a N-**vanillyl fatty acid** amide has a low side-effect and a high antitumor effect, in particular against melanoma and leukemia, and has a very low pungency, a stimulatory and a preinflammatory effect. For example, the reaction of 0.2309 g of **vanillylamine** with 0.5919 of 4,7,10,13,16,19-docosahexaenoic acid (C22:6, DHA) gave 0.311 g of colorless or citrine amorphous-like solid of N-**vanillyl**-4,7,10,13,16,19-docosahexaenamide (Dohevanyl). Antitumor effects of Dohevanyl were compared to those of capsaicin. Compared with capsaicin, Dohevanyl was very low in the degree of hotness and stimulus, and had a higher antitumor effect with a low action to the normal cells. Both capsaicin and Dohevanyl induced apoptosis to cause the cell death.

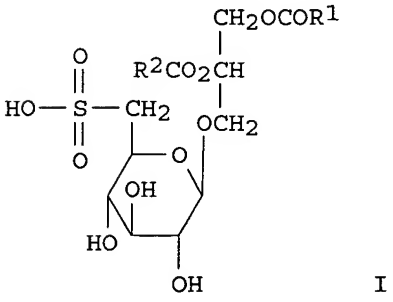
L42 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:272650 HCAPLUS
DOCUMENT NUMBER: 141:99178
TITLE: Effect of capsaicin and N-docosahexaenoyl-**vanillylamide** on growth of taxol-tolerant HeLa cells
AUTHOR(S): Jin, Yongfu; Ishihata, Kimie; Kajiyama, Shin-ichiro; Fukusaki, Ei-ichiro; Kobayashi, Akio; Baba, Naomichi; Tada, Mikiro; **Takahata, Kyoya**
CORPORATE SOURCE: Graduate School of Natural Science and Technology, Okayama University, Japan
SOURCE: Nippon Shokuhin Kagaku Gakkaishi (2002), 9(2), 50-53
CODEN: NSKGF4; ISSN: 1341-2094
PUBLISHER: Nippon Shokuhin Kagaku Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB There are few effective clin. studies to inhibit the growth of multidrug resistance tumor cells. We have been interested in the physiol. actions

of capsaicin (CAP), the pungent ingredient in hot chilli peppers, and polyunsatd. **fatty acids**, for example docosahexaenoic acid (DHA), extracted from fish oil. In this study, we synthesized a new **vanillylamide** derivative, N-docosahexaenoylvanillylamide (dohevanil), to investigate the inhibitory effect of dohevanil on growth of HeLa cells and taxol-tolerant HeLa cells. As a result, dohevanil has more potent inhibitory effect than CAP for both taxol-sensitive HeLa cells and taxol-tolerant HeLa cells. Particularly, the simultaneous addition of dohevanil and taxol more strongly induced cell death of taxol-tolerant HeLa cells. There results obtained in this study suggest that dohevanil has stronger inhibitory effect than CAP for the multidrug resistance cells.

L42 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:843678 HCAPLUS
DOCUMENT NUMBER: 135:376705
TITLE: Brain neuron activators containing sulfoquinovosyldiacylglycerols, and pharmaceutical or food compositions containing them
INVENTOR(S): **Takahata, Kyoya**; Kajita, Keisuke; Osamura, Marina; Tada, Mikio; Haneda, Naohiko; Inoue, Yoshikazu; Araki, Shigeru
PATENT ASSIGNEE(S): Bizen Chemical Co., Ltd., Japan; Yamamoto Nori Ten K. K.
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001322935	A2	20011120	JP 2000-180568	20000512

PRIORITY APPLN. INFO.: JP 2000-180568 20000512
OTHER SOURCE(S): MARPAT 135:376705
GI



I

AB The activators contain sulfoquinovosyldiacylglycerols I (R1, R2 = C14-22 **fatty acid** residue containing 0-6 double bond). A CHCl3-MeOH extract of Porphyra yezoensis was purified by chromatog. to give I (R1 comprises eicosapentaenoic acid 91.0%, arachidonic acid 1.8%, and

palmitic acid 4.6%; R2 comprises 92.5% palmitic acid and 2.8% oleic acid), which promoted neuritogenic activity of NGF and inhibited cell death caused by β-amyloid peptide fragment 25-35.

L42 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:164308 HCAPLUS
DOCUMENT NUMBER: 130:348287
TITLE: Growth inhibition of capsaicin on HeLa cells is not mediated by intracellular calcium mobilization
AUTHOR(S): **Takahata, Kyoya**; Chen, Xiyu; Monobe, Kei-Ichi; Tada, Mikiro
CORPORATE SOURCE: Applied Cell Biochemistry and Cell Culture, Faculty of Agriculture, Okayama University, Okayama, 700-8530, Japan
SOURCE: Life Sciences (1999), 64(13), PL165-PL171
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of capsaicin on cellular growth and intracellular calcium mobilization were examined in human cervical carcinoma derivation, HeLa cells. Capsaicin inhibited cellular growth and increased intracellular calcium level in HeLa cells. This capsaicin-induced intracellular calcium concentration rise was blocked by capsaicin, **vanilloid** (capsaicin) receptor antagonist. But, an intracellular calcium chelator BAPTA/AM did not block the inhibitory effect of capsaicin on cellular growth. These observations suggest that intracellular calcium mobilization is not required for the capsaicin-induced inhibition of cellular growth.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:798578 HCAPLUS
DOCUMENT NUMBER: 130:124255
TITLE: The benefits and risks of n-3 polyunsaturated **fatty acids**
AUTHOR(S): **Takahata, Kyoya**; Monobe, Kei-ichi; Tada, Mikirou; Weber, Peter C.
CORPORATE SOURCE: Faculty of Agriculture, Okayama University, Okayama, 700-8530, Japan
SOURCE: Bioscience, Biotechnology, and Biochemistry (1998), 62(11), 2079-2085
CODEN: BBBIEJ; ISSN: 0916-8451
PUBLISHER: Japan Society for Bioscience, Biotechnology, and Agrochemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 57 refs. There is a growing number of animal models and clin. trials of n-3 polyunsatd. **fatty acid** (PUFAs) supplementation in disease. Epidemiol. and biochem. studies have suggested beneficial effects of n-3 PUFAs. But also, the use of n-3 PUFAs has some potential toxicol. risks that can be circumvented by careless processing, storing, and preserving the PUFAs. The use of n-3 PUFAs is safe if appropriate prepns. and dosages are selected. Much research is needed to clarify their use under different disease conditions. The newly established clin. and nutritional facts on n-3 PUFAs will induce industry to develop food products based on this knowledge.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:288074 HCAPLUS
DOCUMENT NUMBER: 126:324708
TITLE: Pharmacological effects of n-3 polyunsaturated **fatty acids**
AUTHOR(S): **Takahata, Kyoya**; Siess, Wolfgang; Weber, Peter C.
CORPORATE SOURCE: Faculty of Agriculture, Okayama Univ., Okayama, 700, Japan
SOURCE: Foods & Food Ingredients Journal of Japan (1997), 172, 62-70
CODEN: FFIJER; ISSN: 0919-9772
PUBLISHER: FFI Janaru
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 57 refs. There is a constantly increasing number of clin. trials of n-3 **fatty acid** supplementation effects on disease processes. Epidemiol. and biochem. studies have suggested potential anti-inflammatory effect. Moderate clin. benefits have been obtained in patients with rheumatoid arthritis or arterial hypertension. Clearly neg. results have been reported for patients with lupus nephritis, psoriasis or atopic dermatitis. For individuals with coronary artery disease following coronary angioplasty, earlier pos. results of a large meta-anal., could not be confirmed. However, patients with IgA-nephropathy and in those after kidney transplantation, a clear benefit of fish oil application was observed These promising results are currently being pursued in follow-up phase III clin. trials.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:527478 HCAPLUS
DOCUMENT NUMBER: 105:127478
TITLE: Treatment of osteoporosis
INVENTOR(S): Maeda, Yuji; Yamato, Hideyuki; Fujii, Takami; Kobayashi, Yasuhiko; Saito, Kenichi; **Takahata, Kyoya**; Yoshino, Fumiaki; Ubusawa, Masanori; Kato, Tadaaki; Yoshikumi, Chikao
PATENT ASSIGNEE(S): Kureha Chemical Industry Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61109721	A2	19860528	JP 1984-230904	19841101

PRIORITY APPLN. INFO.: JP 1984-230904 19841101
AB 24R,25-Dihydroxycholecalciferol is effective in reducing symptoms (pain) in osteoporosis. Clin. tests confirmed the effectiveness. Capsules were prepared containing 5 mg 24R,25-dihydroxycholecalciferol and 1 kg medium-chain **fatty acid** triglycerides.

Application

L8 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:470289 HCAPLUS
DOCUMENT NUMBER: 141:17594
ENTRY DATE: Entered STN: 10 Jun 2004
TITLE: Antitumor pharmaceutical composition comprising N-vanillyl fatty acid amide
INVENTOR(S): Takahata, Kyoya
PATENT ASSIGNEE(S): Kureha Chemical Industry Company, Limited, Japan
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K031-165
SECONDARY: A61P035-00; A61P035-02
CLASSIFICATION: 1-6 (Pharmacology)
Section cross-reference(s): 25, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1426047	A1	20040609	EP 2003-254668	20030725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2004182674	A2	20040702	JP 2002-353649	20021205
US 2004110844	A1	20040610	US 2003-634641	20030804 <--
PRIORITY APPLN. INFO.:			JP 2002-353649 A	20021205

PATENT CLASSIFICATION CODES:

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 1426047	ICM	A61K031-165
	ICS	A61P035-00; A61P035-02
EP 1426047	ECLA	A61K031/165
JP 2004182674	FTERM	4C206/AA01; 4C206/AA02; 4C206/GA28; 4C206/MA01; 4C206/NA06; 4C206/NA14; 4C206/ZB26
US 2004110844	NCL	514/625.000
	ECLA	A61K031/165 <--

OTHER SOURCE(S): MARPAT 141:17594
ABSTRACT:
The present invention provides an antitumor pharmaceutical composition comprising a N-vanillyl fatty acid amide containing a saturated or unsatd. fatty acid residue containing
14 to 32 carbon atoms which is related to capsaicin. An antitumor pharmaceutical composition comprising a N-vanillyl fatty acid amide has a low side-effect and a high antitumor effect, in particular against melanoma and leukemia, and has a very low pungency, a stimulatory and a preinflammatory effect. For example, the reaction of 0.2309 g of vanillylamine with 0.5919 of 4,7,10,13,16,19-docosahexaenoic acid (C22:6, DHA) gave 0.311 g of colorless or citrine amorphous-like solid of N-vanillyl-4,7,10,13,16,19-docosahexaenamide (Dohevanyl). Antitumor effects of Dohevanyl were compared to those of capsaicin. Compared with capsaicin, Dohevanyl was very low in the degree of hotness and stimulus, and had a higher antitumor effect with a low action to the normal cells. Both capsaicin and Dohevanyl induced apoptosis to cause the cell death.

SUPPL. TERM: vanillyl fatty acid amide prepn antitumor

INDEX TERM: Amides, biological studies
ROLE: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fatty; preparation of antitumor vanillyl fatty acid amides)

INDEX TERM: Antitumor agents
Apoptosis
Human
Leukemia
Melanoma
(preparation of antitumor vanillyl fatty acid amides)

INDEX TERM: **404-86-4**, Capsaicin
ROLE: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); BIOL (Biological study)
(comparison with; preparation of antitumor vanillyl fatty acid amides)

INDEX TERM: **16729-47-8P**, N-Vanillyllinoleamide
58493-49-5P, N-Vanillyloleamide **69693-12-5P**
, N-Vanillylmyristamide **104899-01-6P**
457643-60-6P, N-Vanillylricinoleamide
571203-58-2P, Dohevanil **698373-40-9P**
698373-42-1P
ROLE: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor vanillyl fatty acid amides)

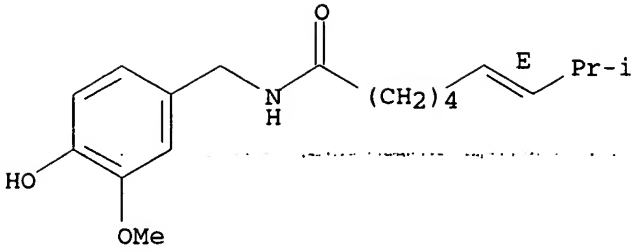
INDEX TERM: **9001-62-1**, Novozyme 435
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of antitumor vanillyl fatty acid amides)

INDEX TERM: **112-62-9**, Methyl oleate **112-63-0**, Methyl linoleate **124-10-7**, Methyl myristate
6217-54-5 7149-10-2, Vanillylamine hydrochloride
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antitumor vanillyl fatty acid amides)

INDEX TERM: **1196-92-5P**, Vanillylamine
ROLE: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor vanillyl fatty acid amides)

IT **404-86-4**, Capsaicin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); BIOL (Biological study)
(comparison with; preparation of antitumor vanillyl fatty acid amides)
RN 404-86-4 HCAPLUS
CN 6-Nonenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-8-methyl-, (6E)- (9CI) (CA INDEX NAME)

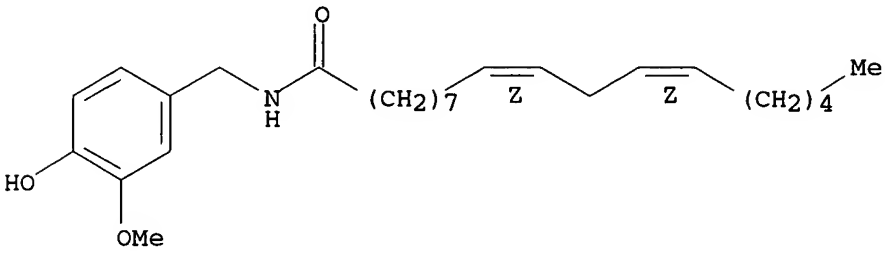
Double bond geometry as shown.



IT **16729-47-8P**, N-Vanillyllinoleamide **58493-49-5P**, N-Vanillyloleamide **69693-12-5P**, N-Vanillylmyristamide **104899-01-6P** **457643-60-6P**, N-Vanillylricinoleamide **571203-58-2P**, Dohevanil **698373-40-9P** **698373-42-1P**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor vanillyl fatty acid amides)

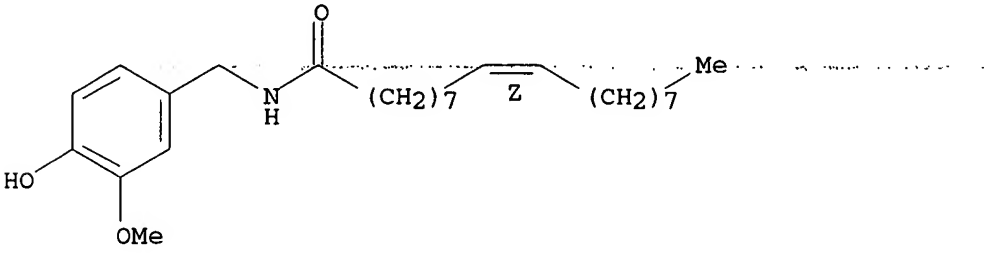
RN 16729-47-8 HCAPLUS
CN 9,12-Octadecadienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

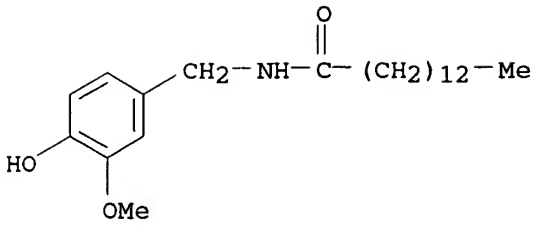


RN 58493-49-5 HCAPLUS
CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

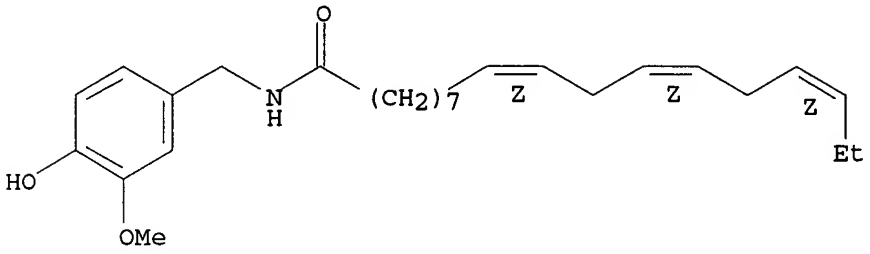


RN 69693-12-5 HCAPLUS
CN Tetradecanamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



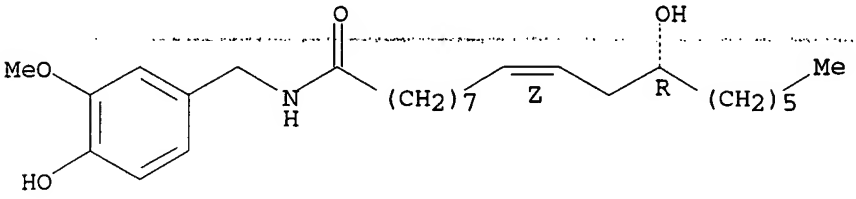
RN 104899-01-6 HCAPLUS
CN 9,12,15-Octadecatrienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12Z,15Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 457643-60-6 HCAPLUS
CN 9-Octadecenamide, 12-hydroxy-N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12R)- (9CI) (CA INDEX NAME)

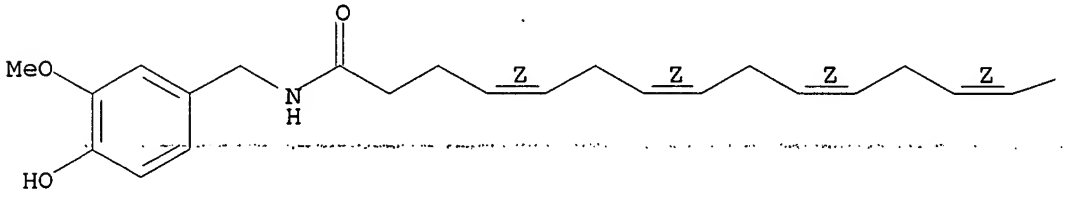
Absolute stereochemistry.
Double bond geometry as shown.



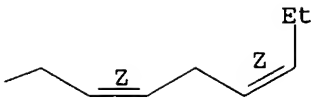
RN 571203-58-2 HCAPLUS
CN 4,7,10,13,16,19-Docosahexaenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (4Z,7Z,10Z,13Z,16Z,19Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

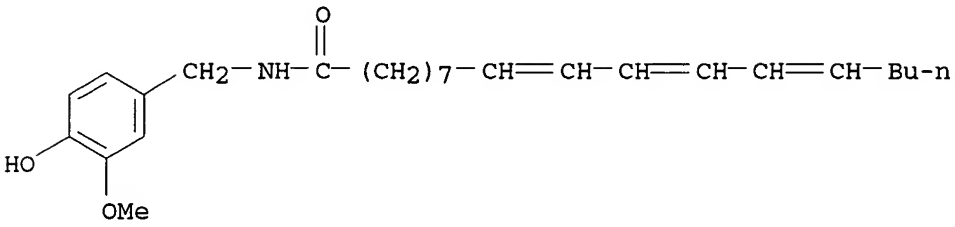
PAGE 1-A



PAGE 1-B



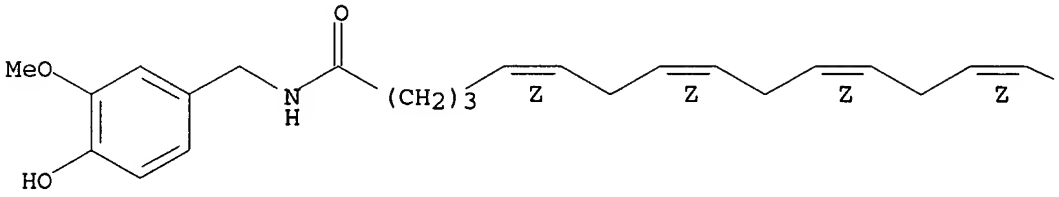
RN 698373-40-9 HCAPLUS
CN 9,11,13-Octadecatrienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



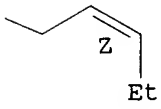
RN 698373-42-1 HCAPLUS
CN 5,8,11,14,17-Eicosapentaenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



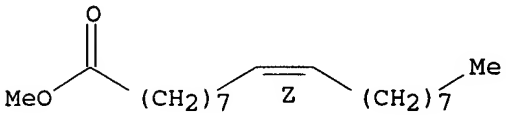
IT **9001-62-1**, Novozyme 435
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of antitumor vanillyl fatty acid amides)
RN 9001-62-1 HCAPLUS
CN Lipase, triacylglycerol (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **112-62-9**, Methyl oleate **112-63-0**, Methyl linoleate
124-10-7, Methyl myristate **6217-54-5 7149-10-2**

, Vanillylamine hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of antitumor vanillyl fatty acid amides)

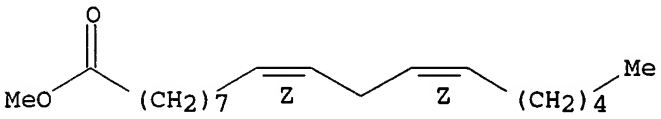
RN 112-62-9 HCAPLUS
CN 9-Octadecenoic acid (9Z)-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

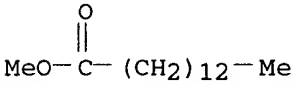


RN 112-63-0 HCAPLUS
CN 9,12-Octadecadienoic acid (9Z,12Z)-, methyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

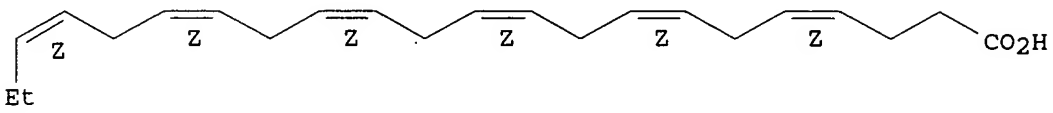


RN 124-10-7 HCAPLUS
CN Tetradecanoic acid, methyl ester (9CI) (CA INDEX NAME)

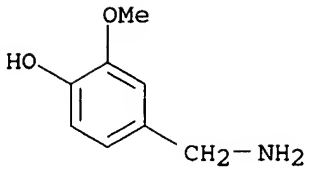


RN 6217-54-5 HCAPLUS
CN 4,7,10,13,16,19-Docosahexaenoic acid, (4Z,7Z,10Z,13Z,16Z,19Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

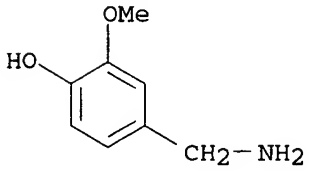


RN 7149-10-2 HCAPLUS
CN Phenol, 4-(aminomethyl)-2-methoxy-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **1196-92-5P**, Vanillylamine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of antitumor vanillyl fatty acid amides)
RN 1196-92-5 HCAPLUS
CN Phenol, 4-(aminomethyl)-2-methoxy- (9CI) (CA INDEX NAME)



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                SEL RN

     FILE 'REGISTRY' ENTERED AT 10:27:10 ON 20 OCT 2005
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                BI OR 457643-60-6/BI OR 571203-58-2/BI OR 58493-49-5/BI OR
                6217-54-5/BI OR 69693-12-5/BI OR 698373-40-9/BI OR 698373-42-1/
                BI OR 7149-10-2/BI OR 9001-62-1/BI)
L3               STR
L4           15 SEA SSS SAM L3
L5               STR L3
L6            1 SEA SSS SAM L5
                D SCA
L7           72 SEA SSS FUL L5

     FILE 'HCAPLUS' ENTERED AT 10:30:07 ON 20 OCT 2005
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                D IALL HITSTR
L9          136 SEA ABB=ON  PLU=ON  L7
L10          82 SEA ABB=ON  PLU=ON  L7(L)(BAC OR DMA OR PAC OR PKT OR THU)/RL
L*** DEL      1 S L1 AND L10
                E ANTITUMOR AGENTS/CT
L11      205779 SEA ABB=ON  PLU=ON  ANTITUMOR AGENTS+PFT/CT
L12          11 SEA ABB=ON  PLU=ON  L10 AND L11
L*** DEL     11 S L9 AND L11
                E MELANOMA/CT
                E E3+ALL
L13      160770 SEA ABB=ON  PLU=ON  MELANOMA+ALL/CT
                E LEUKEMIA/CT
                E E3+ALL
L14       46596 SEA ABB=ON  PLU=ON  LEUKEMIA+PFT,NT,RT/CT
L15           4 SEA ABB=ON  PLU=ON  L12 AND (L13 OR L14 OR MELANOM? OR
                LEUKEM?)
L16           7 SEA ABB=ON  PLU=ON  L9 AND (L13 OR L14 OR MELANOM? OR SKIN
                CANCER OR LEUKEM?)
L17           3 SEA ABB=ON  PLU=ON  L16 NOT L15
                D SCA
                D KWIC
                D KWIC 2-3
L18          14 SEA ABB=ON  PLU=ON  L12 OR L16

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L20           6 SEA ABB=ON  PLU=ON  L19 AND (MELANOM? OR SKIN CANCER? OR
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L21          33 SEA ABB=ON  PLU=ON  L7
                E ANTINEOPLASTIC AG/CT
L22      607330 SEA ABB=ON  PLU=ON  ANTINEOPLASTIC AGENTS+PFT,NT/CT
                E MELANOMA/CT
                E E3+ALL
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L23        47772 SEA ABB=ON  PLU=ON  MELANOMA+PFT,NT/CT
                 E LEUKEMIA
                 E LEUKEMIA/CT
                 E E3+ALL
L24       141267 SEA ABB=ON  PLU=ON  LEUKEMIA+PFT,NT/CT
L25            1 SEA ABB=ON  PLU=ON  L21 AND (L23 OR L24 OR MELANOM? OR LEUKEM?
                 OR SKIN CANCER?)
L26            1 SEA ABB=ON  PLU=ON  L21 AND L22
L27            2 SEA ABB=ON  PLU=ON  L25 OR L26

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L28           97 SEA ABB=ON  PLU=ON  L7
                 E ANTITUMOR AGENT/CT
                 E E3+ALL
                 E E2+ALL
L29        65296 SEA ABB=ON  PLU=ON  ANTINEOPLASTIC AGENTS+PFT/CT
                 E MELANOMA/CT
                 E E3+ALL
L30        43873 SEA ABB=ON  PLU=ON  MELANOMA+PFT,NT/CT
                 E LEUKEMIA/CT
                 E E3+ALL
L31       115097 SEA ABB=ON  PLU=ON  LEUKEMIA+PFT,NT/CT
L32            3 SEA ABB=ON  PLU=ON  L28 AND (L30 OR L31 OR MELANOM? OR
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L33            3 SEA ABB=ON  PLU=ON  L28 AND L29
L34            5 SEA ABB=ON  PLU=ON  L32 OR L33

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     FILE 'WPIX' ENTERED AT 10:45:16 ON 20 OCT 2005

     FILE 'USPATFULL, USPAT2' ENTERED AT 11:00:33 ON 20 OCT 2005
L38           31 SEA ABB=ON  PLU=ON  L7
L39            2 SEA ABB=ON  PLU=ON  L38 AND (MELANOM? OR LEUKEM?)

     FILE 'STNGUIDE' ENTERED AT 11:00:56 ON 20 OCT 2005


     FILE HOME

     FILE HCAPLUS

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FILE COVERS 1907 - 20 Oct 2005 VOL 143 ISS 17
FILE LAST UPDATED: 19 Oct 2005 (20051019/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 OCT 2005 HIGHEST RN 865652-03-5
DICTIONARY FILE UPDATES: 19 OCT 2005 HIGHEST RN 865652-03-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE MEDLINE
FILE LAST UPDATED: 19 OCT 2005 (20051019/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE
FILE COVERS 1974 TO 13 Oct 2005 (20051013/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 19 October 2005 (20051019/ED)

FILE RELOADED: 19 October 2003.

FILE PROUSDDR

FILE COVERS 1980 TO 3 Oct 2005 (20051003/ED)

FILE WPIX
FILE LAST UPDATED: 19 OCT 2005 <20051019/UP>
MOST RECENT DERWENT UPDATE: 200567 <200567/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-rev FOR DETAILS. <<<

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 Oct 2005 (20051018/PD)
FILE LAST UPDATED: 18 Oct 2005 (20051018/ED)
HIGHEST GRANTED PATENT NUMBER: US6957446
HIGHEST APPLICATION PUBLICATION NUMBER: US2005229280
CA INDEXING IS CURRENT THROUGH 18 Oct 2005 (20051018/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Oct 2005 (20051018/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<

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>>> original, i.e., the earliest published granted patents or          <<<
>>> applications.  USPAT2 contains full text of the latest US          <<<
>>> publications, starting in 2001, for the inventions covered in      <<<
>>> USPATFULL.  A USPATFULL record contains not only the original      <<<
>>> published document but also a list of any subsequent               <<<
>>> publications.  The publication number, patent kind code, and       <<<
>>> publication date for all the US publications for an invention      <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL    <<<
>>> records and may be searched in standard search fields, e.g., /PN,  <<<
>>> /PK, etc.                                                          <<<

>>> USPATFULL and USPAT2 can be accessed and searched together         <<<
>>> through the new cluster USPATALL.  Type FILE USPATALL to           <<<
>>> enter this cluster.                                               <<<
>>>                                                                   <<<
>>> Use USPATALL when searching terms such as patent assignees,       <<<
>>> classifications, or claims, that may potentially change from      <<<
>>> the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

FILE USPAT2

FILE COVERS 2001 TO PUBLICATION DATE: 18 Oct 2005 (20051018/PD)
FILE LAST UPDATED: 18 Oct 2005 (20051018/ED)
HIGHEST GRANTED PATENT NUMBER: US2004187682
HIGHEST APPLICATION PUBLICATION NUMBER: US2005229256
CA INDEXING IS CURRENT THROUGH 18 Oct 2005 (20051018/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Oct 2005 (20051018/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED:  Aug 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2005

USPAT2 is a companion file to USPATFULL.  USPAT2 contains full text
of the latest US publications, starting in 2001, for the inventions
covered in USPATFULL.  USPATFULL contains full text of the original
published US patents from 1971 to date and the original applications
from 2001.  In addition, a USPATFULL record for an invention contains
a complete list of publications that may be searched in standard
search fields, e.g., /PN, /PK, etc.

USPATFULL and USPAT2 can be accessed and searched together through
the new cluster USPATALL.  Type FILE USPATALL to enter this cluster.

Use USPATALL when searching terms such as patent assignees,
classifications, or claims, that may potentially change from the
earliest to the latest publication.

FILE STNGUIDE
FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 14, 2005 (20051014/UP).

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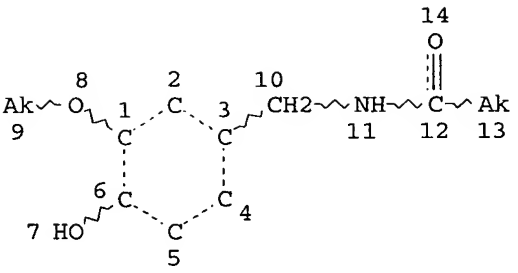

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DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 9
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ECOUNT IS M13 C AT 13

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

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L9	136	SEA FILE=HCAPLUS ABB=ON	PLU=ON L7
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L11	205779	SEA FILE=HCAPLUS ABB=ON	PLU=ON ANTITUMOR AGENTS+PFT/CT
L12	11	SEA FILE=HCAPLUS ABB=ON	PLU=ON L10 AND L11
L13	160770	SEA FILE=HCAPLUS ABB=ON	PLU=ON MELANOMA+ALL/CT
L14	46596	SEA FILE=HCAPLUS ABB=ON	PLU=ON LEUKEMIA+PFT,NT,RT/CT
L16	7	SEA FILE=HCAPLUS ABB=ON	PLU=ON L9 AND (L13 OR L14 OR MELANOM? OR SKIN CANCER OR LEUKEM?)
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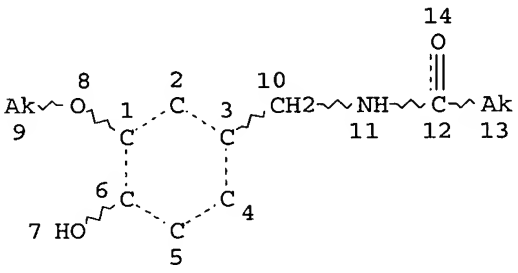

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DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M13 C AT 13

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS  14

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                 T
L23        47772 SEA FILE=MEDLINE ABB=ON  PLU=ON  MELANOMA+PFT,NT/CT
L24       141267 SEA FILE=MEDLINE ABB=ON  PLU=ON  LEUKEMIA+PFT,NT/CT
L25            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L21 AND (L23 OR L24 OR
                   MELANOM? OR LEUKEM? OR SKIN CANCER?)
L26            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L21 AND L22
L27            2 SEA FILE=MEDLINE ABB=ON  PLU=ON  L25 OR L26


=> d que stat l34
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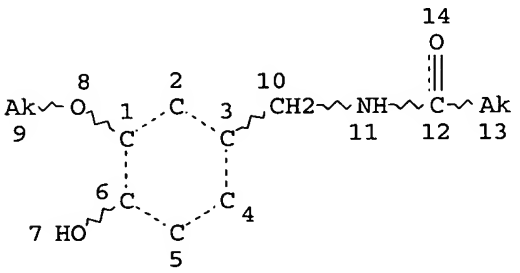


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L29        65296 SEA FILE=EMBASE ABB=ON  PLU=ON  ANTINEOPLASTIC AGENTS+PFT/CT
L30        43873 SEA FILE=EMBASE ABB=ON  PLU=ON  MELANOMA+PFT,NT/CT
L31       115097 SEA FILE=EMBASE ABB=ON  PLU=ON  LEUKEMIA+PFT,NT/CT
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                   MELANOM? OR LEUKEM?)
L33            3 SEA FILE=EMBASE ABB=ON  PLU=ON  L28 AND L29
L34            5 SEA FILE=EMBASE ABB=ON  PLU=ON  L32 OR L33


=> d que stat l36
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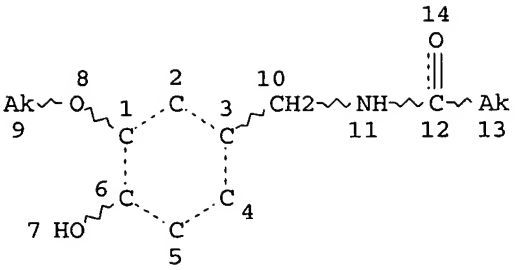

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CONNECT IS E1 RC AT 9
DEFAULT MLEVEL IS ATOM
GGCAT IS LOC AT 9
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DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M13 C AT 13

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L7 72 SEA FILE=REGISTRY SSS FUL L5
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=> d que stat l39
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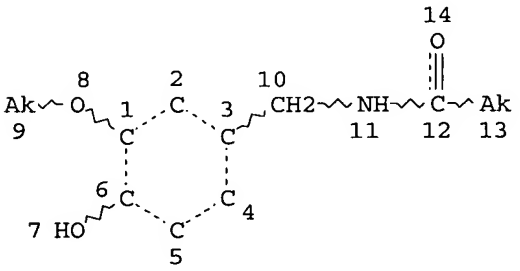

NODE ATTRIBUTES:
CONNECT IS E1 RC AT 9
DEFAULT MLEVEL IS ATOM
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GGCAT IS HIC AT 13
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M13 C AT 13

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE
L7 72 SEA FILE=REGISTRY SSS FUL L5

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PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L36
PROCESSING COMPLETED FOR L39
L40          16 DUP REM L18 L27 L34 L36 L39 (9 DUPLICATES REMOVED)
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                ANSWER '15' FROM FILE EMBASE
                ANSWER '16' FROM FILE USPATFULL

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L40  ANSWER 1 OF 16  HCAPLUS  COPYRIGHT 2005 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2004:513343  HCAPLUS
DOCUMENT NUMBER:          141:71387
TITLE:                    Preparation of anandamide and arvanil analogs as
                          potential analgesics which bind CR1 and VR1
INVENTOR(S):              Martin, Billy R.; Razdan, Raj K.; Di Marzo, Vincenzo
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 25 pp., Cont.-in-part of U.S.
                          Ser. No. 170,204.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2004122089         A1    20040624    US 2003-365607          20030213
PRIORITY APPLN. INFO.:                       US 2001-299199P      P  20010620
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OTHER SOURCE(S):          MARPAT 141:71387
GI
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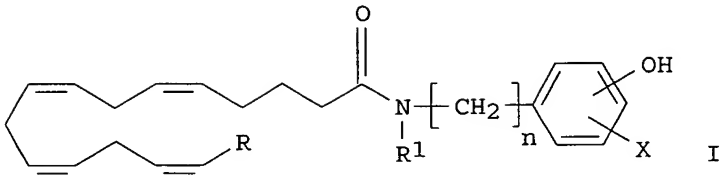

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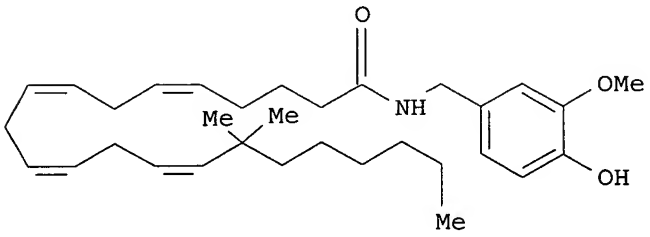


II

AB Analogs of anandamide and arvanil of formula I (n = 0-5, X = H, C1-6 alkyl, halogen, hydroxy, or C1-6 alkoxy, R1 = H, C1-6 alkyl, R = substituted alkyl) were prepared as analgesic agents which bind to CB1 and VR1 receptors. Thus, but-2-yn-1,4-diol was treated with K2CO3, CuI, NaI and Me hex-5-ynoate to give the 1-hydroxy-deca-5,8-diynoic acid Me ester which was treated with but-3-yn-4-ol to give the corresponding trynoic acid Me ester. The trynoic ester was reduced to the trienoic acid Me ester using Ni(OAc)2, ethylenediamine, and NaBH4 in EtOH, and then treated with triphenylphosphine, imidazole, and I2 to give Me 14-triphenylphosphino-tetradeca-all-cis-5,8,11-trienoate iodide. This iodide was reacted with the corresponding aldehyde to give 16,16-dimethyl-docosa-5,8,11,14-all-cis-tetraenoic acid Me ester which upon conversion of the acid and reaction with 4-hydroxy-3-methoxy benzyl amine yielded II. II had an EC50 of 0.7 nM against the VR1 and a Ki of 261.8 nM for CB1. The analogs provide analgesic effects in vivo, and are useful in pain management. In addition, the analogs may be used as anti-proliferative/anti-tumor agents, vasodilators, and in other applications. Several of the anandamide and arvanil analogs are more potent than anandamide and arvanil.

IC ICM C11C003-00
ICS A61K031-277; A61K031-16

INCL 514509000; 514521000; 514627000; 554051000; 554054000

CC 26-3 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 63

IT Analgesics
Anti-inflammatory agents
Antitumor agents
Cytotoxic agents
Human
Neoplasm
Vasodilators
(preparation of analogs of eicosanoid analogs of anandamide and arvanil as analgesics, antiinflammatories, vasodilators, and antiproliferatives which bind to CB1 or VR1 receptors)

IT 94421-68-8DP, Anandamide, analogs **128007-31-8DP**, Arvanil, analogs **322399-51-9P 322399-54-2P 322399-59-7P**
322399-60-0P 342882-76-2P 342882-77-3P 342882-78-4P
439079-98-8P 439079-99-9P 439080-00-9P 439080-02-1P 439080-03-2P
439080-04-3P 439080-05-4P 710294-67-0P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP

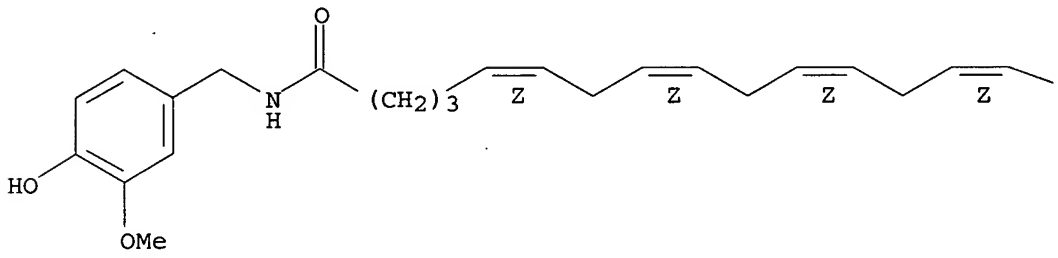
(Preparation); USES (Uses)
(preparation of analogs of eicosanoid analogs of anandamide and arvanil as analgesics, antiinflammatories, vasodilators, and antiproliferatives which bind to CB1 or VR1 receptors)

IT **128007-31-8DP**, Arvanil, analogs **322399-51-9P**
322399-54-2P 322399-59-7P 322399-60-0P
RL: **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of analogs of eicosanoid analogs of anandamide and arvanil as analgesics, antiinflammatories, vasodilators, and antiproliferatives which bind to CB1 or VR1 receptors)

RN 128007-31-8 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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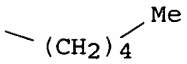
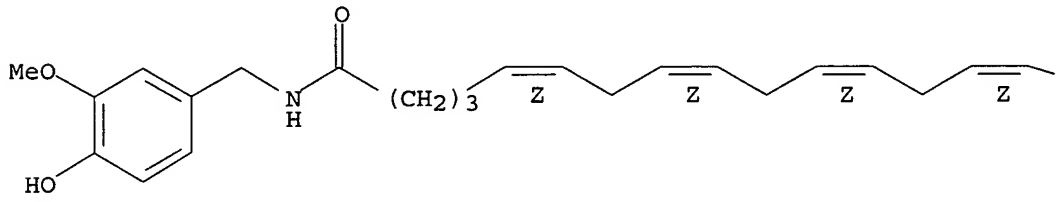


RN 322399-51-9 HCAPLUS
CN 5,8,11,14-Docosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-16,16-dimethyl-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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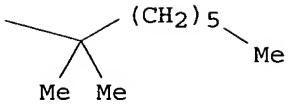
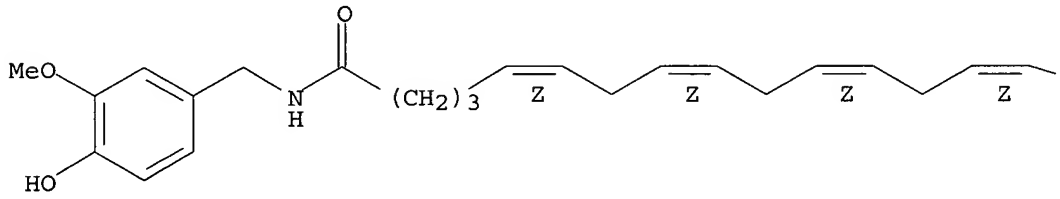


RN 322399-54-2 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, 20-hydroxy-N-[(4-hydroxy-3-methoxyphenyl)methyl]-16,16-dimethyl-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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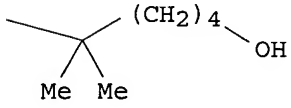
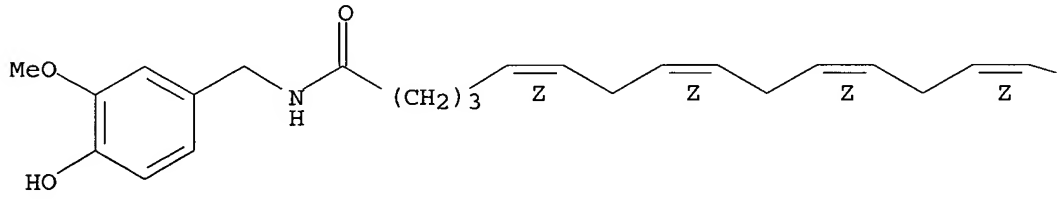


RN 322399-59-7 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, 20-bromo-N-[(4-hydroxy-3-methoxyphenyl)methyl]-16,16-dimethyl-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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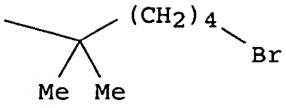
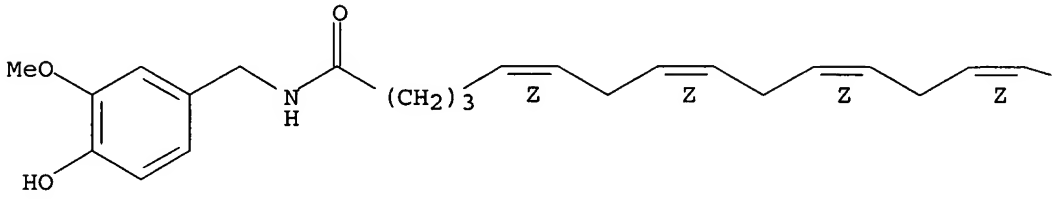


RN 322399-60-0 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, 20-cyano-N-[(4-hydroxy-3-methoxyphenyl)methyl]-16,16-dimethyl-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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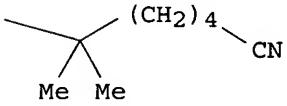


L40 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:815183 HCAPLUS
DOCUMENT NUMBER: 141:343063
TITLE: A new strategy to block tumor growth by inhibiting endocannabinoid inactivation
AUTHOR(S): Bifulco, Maurizio; Laezza, Chiara; Valenti, Marta; Ligresti, Alessia; Portella, Giuseppe; Di Marzo, Vincenzo
CORPORATE SOURCE: Endocannabinoid Research Group, Universita degli Studi di Salerno, Pozzuoli, 80078, Italy
SOURCE: FASEB Journal (2004), 18(13), 1606-1608, 10.1096/fj.04-1754fje
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Endocannabinoid signaling has been shown to be enhanced in several cancer tissues and malignant cells, and studies in cell lines have shown that this up-regulation might serve the purpose of providing transformed cells with a further means to inhibit their proliferation. Here the authors investigated the effect of inhibitors of endocannabinoid degradation on the

growth of rat thyroid tumor xenografts induced in athymic mice. VDM-11, a selective inhibitor of endocannabinoid cellular reuptake, and arachidonoyl-serotonin (AA-5-HT), a selective blocker of endocannabinoid enzymic hydrolysis, both inhibited the growth in vivo of tumor xenografts induced by the s.c. injection of rat thyroid transformed (KiMol) cells. This effect was accompanied by significantly enhanced endocannabinoid concns. in the tumors excised at the end of the in vivo expts. Endocannabinoids, as well as VDM-11 and AA-5-HT, inhibited the growth in vitro of the transformed rat thyroid cells used to induce the tumors in vivo, and their effect was reversed at least in part by the cannabinoid CB1 receptor antagonist SR141716A. This compound, however, when administered alone, did not enhance, but instead slightly inhibited, the growth of rat thyroid transformed cells both in vitro and in tumor xenografts induced in vivo. These findings indicate that endocannabinoids tonically control tumor growth in vivo by both CB1-mediated and non-CB1-mediated mechanisms and that, irresp. of the mol. mechanism of their antiproliferative action, inhibitors of their inactivation might be used for the development of novel anticancer drugs.

CC 1-6 (Pharmacology)

IT **Antitumor agents**
Thyroid gland, neoplasm
(new strategy to block tumor growth by inhibiting endocannabinoid inactivation)

IT **128007-31-8**, Arvanil 158681-13-1, SR141716A 166100-39-6
187947-37-1 313998-81-1, VDM-11
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(new strategy to block tumor growth by inhibiting endocannabinoid inactivation)

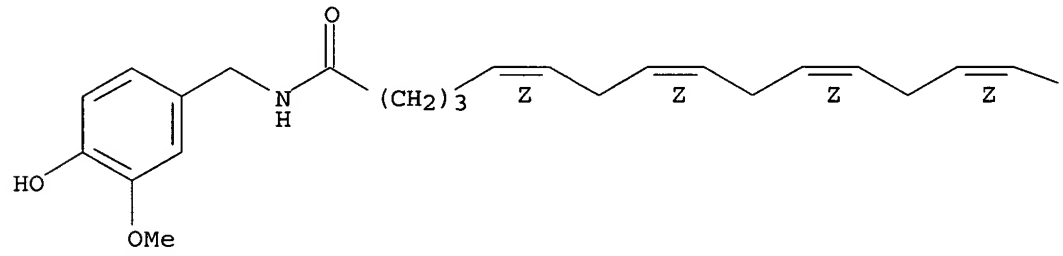
IT **128007-31-8**, Arvanil
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(new strategy to block tumor growth by inhibiting endocannabinoid inactivation)

RN 128007-31-8 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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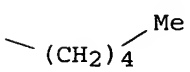

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L40 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2003:955404 HCAPLUS
DOCUMENT NUMBER: 140:104702
TITLE: The CB1/VR1 agonist arvanil induces apoptosis through an FADD/caspase-8-dependent pathway
AUTHOR(S): Sancho, Rocio; de la Vega, Laureano; Appendino, Giovanni; Di Marzo, Vincenzo; Macho, Antonio; Munoz, Eduardo
CORPORATE SOURCE: Departamento de Biologia Celular, Fisiologia e Inmunologia, Universidad de Cordoba, Facultad de Medicina, Cordoba, 14004, Spain
SOURCE: British Journal of Pharmacology (2003), 140(6), 1035-1044 Nov./2003
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 Arvanil (N-arachidonoylvanillamine), a nonpungent capsaicin-anandamide hybrid mol., has been shown to exert biol. activities through VR1/CB1-dependent and -independent pathways. The authors have found that arvanil induces dose-dependent apoptosis in the lymphoid Jurkat T-cell line, but not in peripheral blood T lymphocytes. Apoptosis was assessed by DNA fragmentation through cell cycle and TUNEL analyses. 2 Arvanil-induced apoptosis was initiated independently of any specific phase of the cell cycle, and it was inhibited by specific caspase-8 and -3 inhibitors and by the activation of protein kinase C. In addition, kinetic anal. by Western blots and fluorometry showed that arvanil rapidly activates caspase-8, -7 and -3, and induces PARP cleavage. 3 The arvanil-mediated apoptotic response was greatly inhibited in the Jurkat-FADDDN cell line, which constitutively expresses a neg. dominant form of the adapter mol. Fas-associated death domain (FADD). This cell line does not undergo apoptosis in response to Fas (CD95) stimulation. 4 Using a cytofluorimetric approach, the authors have found that arvanil induced the production of reactive oxygen species (ROS) in both Jurkat-FADD+ and Jurkat-FADDDN cell lines. However, ROS accumulation only plays a residual role in arvanil-induced apoptosis. 5 These results demonstrate that arvanil-induced apoptosis is essentially mediated through a mechanism that is typical of type II cells, and implicates the death-inducing signaling complex and the activation of caspase-8. This arvanil-apoptotic activity is TRPV1 and CB-independent, and can be of importance for the development of potential anti-inflammatory and antitumoral drugs.

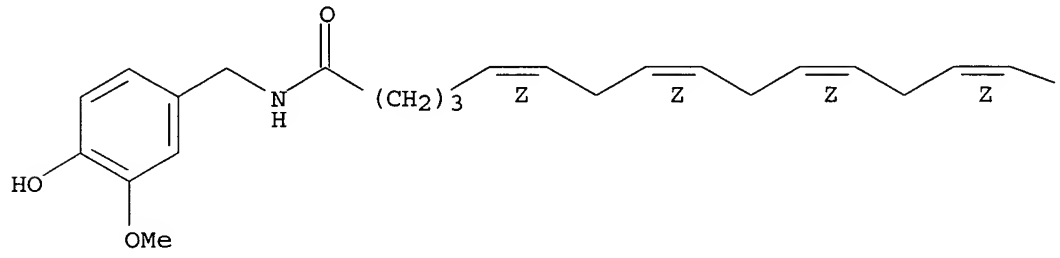
CC 1-6 (Pharmacology)
IT **Antitumor agents**
Apoptosis
Human
Leukemia
Signal transduction, biological
(CB1/VR1 agonist arvanil induces apoptosis through an FADD/caspase-dependent pathway)
IT **128007-31-8**, Arvanil
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CB1/VR1 agonist arvanil induces apoptosis through an FADD/caspase-dependent pathway)
IT **128007-31-8**, Arvanil

RL: **DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(CB1/VR1 agonist arvanil induces apoptosis through an FADD/caspase-dependent pathway)

RN 128007-31-8 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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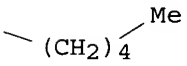


REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2002:815936 HCAPLUS
DOCUMENT NUMBER: 138:331324
TITLE: Effect on cancer cell proliferation of palmitoylethanolamide, a fatty acid amide interacting with both the cannabinoid and vanilloid signalling systems
AUTHOR(S): De Petrocellis, Luciano; Bisogno, Tiziana; Ligresti, Alessia; Bifulco, Maurizio; Melck, Dominique; Di Marzo, Vincenzo
CORPORATE SOURCE: Endocannabinoid Research Group, Istituto di Cibernetica "Eduardo Caianiello" Consiglio Nazionale delle Ricerche, Comprensorio Olivetti, Naples, Italy
SOURCE: Fundamental & Clinical Pharmacology (2002), 16(4), 297-302
CODEN: FCPHEZ; ISSN: 0767-3981
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Following a discussion of recent literature on palmitoylethanolamide (PEA) and data on the possible mechanism(s) of its anti-inflammatory and analgesic effects, new data are presented which suggest that PEA can enhance the antiproliferative effects of type 1 vanilloid receptor agonists (possibly including anandamide), although by a mechanism

different from that previously suggested to underlie the enhancement of the cytostatic actions of anandamide/cannabinoids. Although the relative involvement of cannabinoid and vanilloid receptors in the control of cancer cell division, differentiation and apoptosis still needs to be fully investigated, this "entourage" effect of PEA might be used therapeutically if agonists at these receptors are used as antitumor agents. PEA could be coadministered with either anandamide or capsaicin derivs. to lower the threshold of the antitumor effects of these compds. to doses that do not produce undesired psychotropic activity or pungency/toxicity, resp.

CC 1-6 (Pharmacology)

IT **Antitumor agents**
(breast cancer; palmitoylethanolamide, a fatty acid amide interacting with both the cannabinoid and vanilloid signalling systems, effect on cancer cell proliferation)

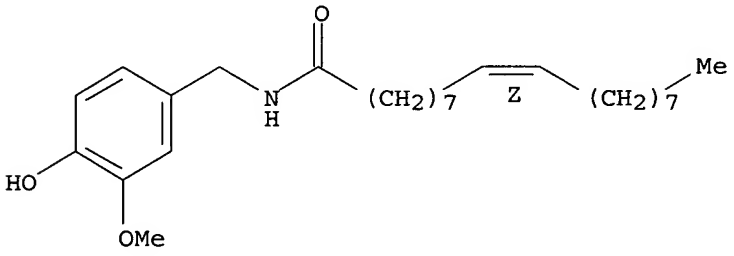
IT 404-86-4, Capsaicin 57444-62-9, Resiniferatoxin **58493-49-5**, Olvanil
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(palmitoylethanolamide, a fatty acid amide interacting with both the cannabinoid and vanilloid signalling systems, effect on the antiproliferative effect of)

IT **58493-49-5**, Olvanil
RL: BSU (Biological study, unclassified); **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(palmitoylethanolamide, a fatty acid amide interacting with both the cannabinoid and vanilloid signalling systems, effect on the antiproliferative effect of)

RN 58493-49-5 HCAPLUS

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2001:322837 HCAPLUS

DOCUMENT NUMBER: 135:132395

TITLE: Characterization of palmitoylethanolamide transport in mouse Neuro-2a neuroblastoma and rat RBL-2H3 basophilic leukaemia cells: comparison with anandamide

AUTHOR(S): Jacobsson, Stig O. P.; Fowler, Christopher J.

CORPORATE SOURCE: Department of Pharmacology and Clinical Neuroscience, Department of Odontology, Umea University, Umea,

SE-901 87, Swed.
SOURCE: British Journal of Pharmacology (2001), 132(8), 1743-1754
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The endogenous cannabinoid receptor agonist anandamide (AEA) and the related compound palmitoylethanolamide (PEA) are inactivated by transport into cells followed by metabolism by fatty acid amide hydrolase (FAAH). The cellular uptake of AEA has been characterized in detail, whereas less is known about the properties of the PEA uptake, in particular in neuronal cells. In the present study, the pharmacol. and functional properties of PEA and AEA uptake have been investigated in mouse Neuro-2a neuroblastoma and, for comparison, in rat RBL-2H3 basophilic **leukemia** cells. Saturable uptake of PEA and AEA into both cell lines were demonstrated with apparent KM values of 28 μM (PEA) and 10 μM (AEA) in Neuro-2a cells, and 30 μM (PEA) and 9.3 μM (AEA) in RBL-2H3 cells. Both PEA and AEA uptake showed temperature-dependence but only the AEA uptake was sensitive to treatment with Pronase and phenylmethylsulfonyl fluoride. The AEA uptake was inhibited by AM404, 2-arachidonoylglycerol (2-AG), R1- and S1-methanandamide, arachidonic acid and olvanil with similar potencies for the two cell types. PEA, up to a concentration of 100 μM, did not affect AEA uptake in either cell line. AEA, 2-AG, arachidonic acid, R1-methanandamide, Δ9-THC, and cannabidiol inhibited PEA transport in both cell lines. The non-steroidal anti-inflammatory drug indomethacin inhibited the AEA uptake but had very weak effects on the uptake of PEA. From these data, it can be concluded that PEA is transported in to cells both by passive diffusion and by a facilitated transport that is pharmacol. distinguishable from AEA uptake.

CC 1-12 (Pharmacology)
Section cross-reference(s): 2, 13

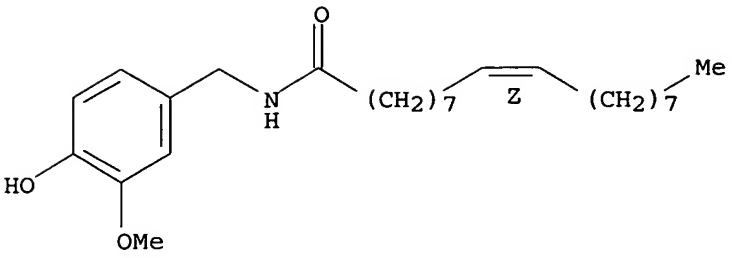
IT 53-86-1, Indomethacin 329-98-6, Phenylmethylsulfonyl fluoride 506-32-1, Arachidonic acid 1972-08-3, Δ9-THC 9036-06-0, Pronase 13956-29-1, Cannabidiol 15687-27-1, Ibuprofen 53847-30-6 **58493-49-5**, Olvanil 157182-49-5, R-Methanandamide 157182-50-8, S-Methanandamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. characterization of palmitoylethanolamide transport in neuronal cells)

IT **58493-49-5**, Olvanil
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. characterization of palmitoylethanolamide transport in neuronal cells)

RN 58493-49-5 HCAPLUS

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1998:698015 HCAPLUS
DOCUMENT NUMBER: 130:76092
TITLE: Interactions between synthetic vanilloids and the endogenous cannabinoid system
AUTHOR(S): Di Marzo, Vincenzo; Bisogno, Tiziana; Melck, Dominique; Ross, Ruth; Brockie, Heather; Stevenson, Lesley; Pertwee, Roger; De Petrocellis, Luciano
CORPORATE SOURCE: Istituto per la Chimica di Molecole di Interesse Biologico, CNR, Arco Felice, 80072, Italy
SOURCE: FEBS Letters (1998), 436(3), 449-454
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chemical similarity between some synthetic agonists of vanilloid receptors, such as olvanil (N-vanillyl-cis-9-octadecenoamide), and the 'endocannabinoid' anandamide (arachidonoyl-ethanolamide, AEA), suggests possible interactions between the cannabinoid and vanilloid signalling systems. Here the authors report that olvanil is a stable and potent inhibitor of AEA facilitated transport into rat basophilic **leukemia** (RBL-2H3) cells. Olvanil blocked both the uptake and the hydrolysis of [14C]AEA by intact RBL-2H3 cells (IC50 = 9 μM), while capsaicin and pseudocapsaicin (N-vanillyl-nonanamide) were much less active. Olvanil was more potent than previously reported inhibitors of AEA facilitated transport, i.e. phloretin (IC50 = 80 μM), AM404 (12.9%, inhibition at 10 μM) or oleoylethanolamide (27.5% inhibition at 10 μM). Olvanil was a poor inhibitor of [14C]AEA hydrolysis by RBL-2H3 and N18TG2 cell membranes, suggesting that the inhibitory effect on [14C]AEA breakdown observed in intact cells was due to inhibition of [14C]AEA uptake. Olvanil was stable to enzymic hydrolysis, and (i) displaced the binding of high affinity cannabinoid receptor ligands to membrane prepns. from N18TG2 cells and guinea pig forebrain (Ki = 1.64-7.08 μM), but not from cells expressing the CB2 cannabinoid receptor subtype; (ii) inhibited forskolin-induced cAMP formation in intact N18TG2 cells (IC50 = 1.60 μM), this effect being reversed by the selective CB1 antagonist SR141716A. Pseudocapsaicin, but not capsaicin, also selectively bound to CB1 receptor-containing membranes. These data suggest that some of the analgesic actions of olvanil may be due to its interactions with the endogenous cannabinoid system, and may lead to the design of a novel class of cannabimimetics with potential therapeutic applications as analgesics.

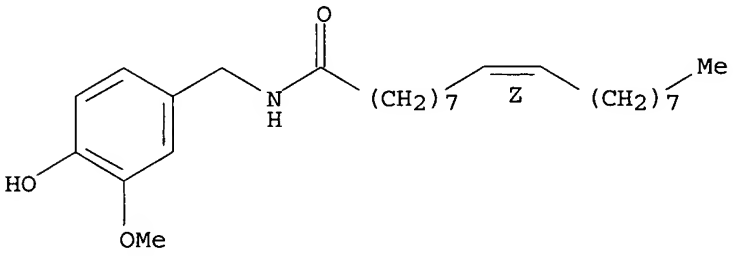
CC 1-11 (Pharmacology)
Section cross-reference(s): 2
IT 60-82-2, Phloretin 111-58-0 404-86-4, Capsaicin 2444-46-4, Pseudocapsaicin **58493-49-5**, Olvanil 94421-68-8, Anandamide

183718-77-6, AM 404
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interactions between synthetic vanilloids and the endogenous cannabinoid system)

IT **58493-49-5**, Olvanil
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(interactions between synthetic vanilloids and the endogenous cannabinoid system)

RN 58493-49-5 HCAPLUS
CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:470289 HCAPLUS
DOCUMENT NUMBER: 141:17594
TITLE: Antitumor pharmaceutical composition comprising N-vanillyl fatty acid amide
INVENTOR(S): Takahata, Kyoya
PATENT ASSIGNEE(S): Kureha Chemical Industry Company, Limited, Japan
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1426047	A1	20040609	EP 2003-254668	20030725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2004182674	A2	20040702	JP 2002-353649	20021205
US 2004110844	A1	20040610	US 2003-634641	20030804
PRIORITY APPLN. INFO.:			JP 2002-353649 A	20021205

OTHER SOURCE(S): MARPAT 141:17594
AB The present invention provides an antitumor pharmaceutical composition comprising a N-vanillyl fatty acid amide containing a saturated or unsatd. fatty
acid residue containing 14 to 32 carbon atoms which is related to capsaicin.

An antitumor pharmaceutical composition comprising a N-vanillyl fatty acid amide has a low side-effect and a high antitumor effect, in particular against **melanoma** and **leukemia**, and has a very low pungency, a stimulatory and a preinflammatory effect. For example, the reaction of 0.2309 g of vanillylamine with 0.5919 of 4,7,10,13,16,19-docosahexaenoic acid (C22:6, DHA) gave 0.311 g of colorless or citrine amorphous-like solid of N-vanillyl-4,7,10,13,16,19-docosahexaenamide (Dohevanyl). Antitumor effects of Dohevanyl were compared to those of capsaicin. Compared with capsaicin, Dohevanyl was very low in the degree of hotness and stimulus, and had a higher antitumor effect with a low action to the normal cells. Both capsaicin and Dohevanyl induced apoptosis to cause the cell death.

IC ICM A61K031-165
ICS A61P035-00; A61P035-02

CC 1-6 (Pharmacology)
Section cross-reference(s): 25, 63

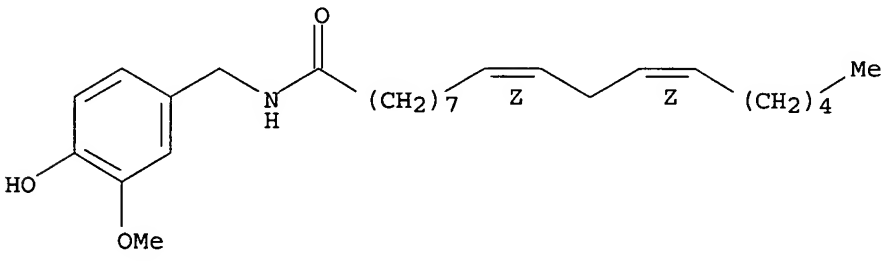
IT **Antitumor agents**
Apoptosis
Human
Leukemia
Melanoma
(preparation of antitumor vanillyl fatty acid amides)

IT **16729-47-8P**, N-Vanillyllinoleamide **58493-49-5P**, N-Vanillyloleamide **69693-12-5P**, N-Vanillylmyristamide **104899-01-6P 457643-60-6P**, N-Vanillylricinoleamide **571203-58-2P**, Dohevanil **698373-40-9P** **698373-42-1P**
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor vanillyl fatty acid amides)

IT **16729-47-8P**, N-Vanillyllinoleamide **58493-49-5P**, N-Vanillyloleamide **69693-12-5P**, N-Vanillylmyristamide **104899-01-6P 457643-60-6P**, N-Vanillylricinoleamide **571203-58-2P**, Dohevanil **698373-40-9P** **698373-42-1P**
RL: ADV (Adverse effect, including toxicity); **PAC (Pharmacological activity)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antitumor vanillyl fatty acid amides)

RN 16729-47-8 HCAPLUS
CN 9,12-Octadecadienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12Z)-(9CI) (CA INDEX NAME)

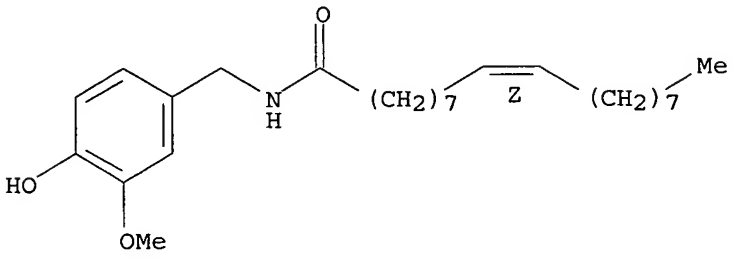
Double bond geometry as shown.



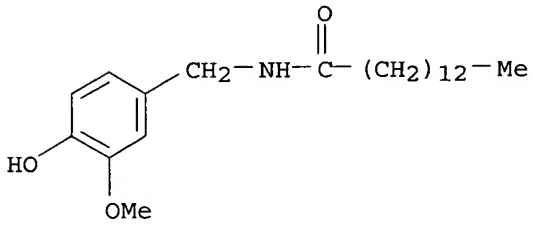
RN 58493-49-5 HCAPLUS
CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA

INDEX NAME)

Double bond geometry as shown.

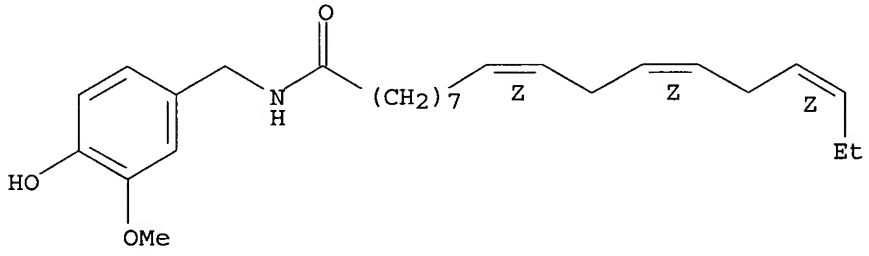


RN 69693-12-5 HCAPLUS
CN Tetradecanamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



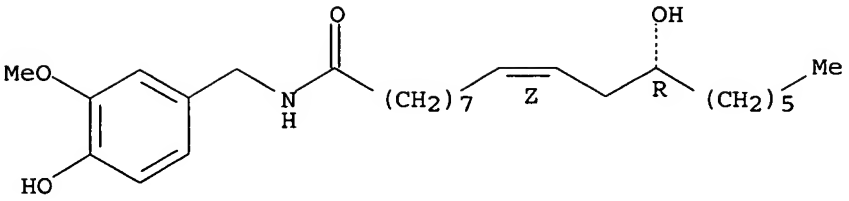
RN 104899-01-6 HCAPLUS
CN 9,12,15-Octadecatrienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12Z,15Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 457643-60-6 HCAPLUS
CN 9-Octadecenamide, 12-hydroxy-N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12R)- (9CI) (CA INDEX NAME)

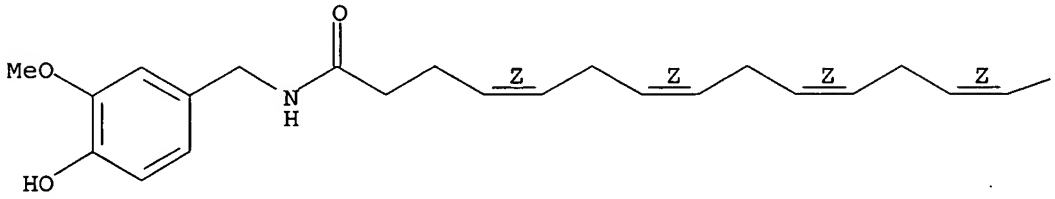
Absolute stereochemistry.
Double bond geometry as shown.



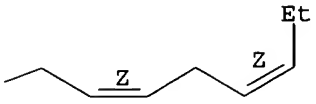
RN 571203-58-2 HCAPLUS
CN 4,7,10,13,16,19-Docosahexaenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (4Z,7Z,10Z,13Z,16Z,19Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

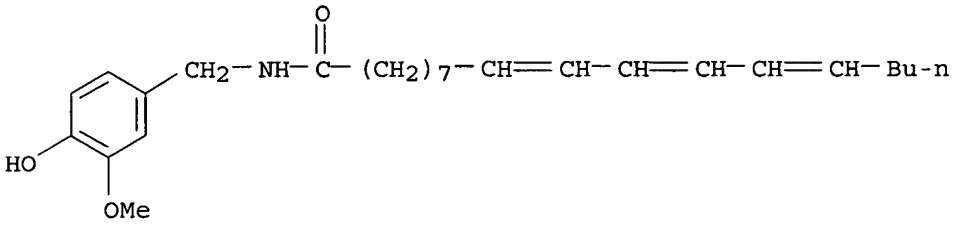
PAGE 1-A



PAGE 1-B



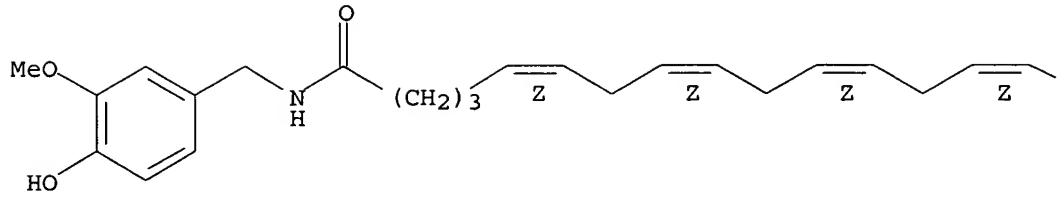
RN 698373-40-9 HCAPLUS
CN 9,11,13-Octadecatrienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



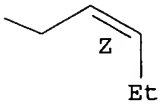
RN 698373-42-1 HCAPLUS
CN 5,8,11,14,17-Eicosapentaenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L40 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:468924 HCAPLUS
DOCUMENT NUMBER: 141:68639
TITLE: Further evidence for the existence of a specific process for the membrane transport of anandamide
AUTHOR(S): Ligresti, Alessia; Morera, Enrico; Van Der Stelt, Mario; Monory, Krisztina; Lutz, Beat; Ortar, Giorgio; Di Marzo, Vincenzo
CORPORATE SOURCE: Endocannabinoid Research Group, Institute of Biomolecular Chemistry, National Research Council, Pozzuoli, 80078, Italy
SOURCE: Biochemical Journal (2004), 380(1), 265-272
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Indirect evidence for the existence of a specific protein-mediated process for the cellular uptake of endocannabinoids has been reported, but recent results suggested that such a process, at least for AEA [N-arachidonoylethanolamine (anandamide)], is facilitated uniquely by its intracellular hydrolysis by FAAH (fatty acid amide hydrolase) [Glaser, Abumrad, Fatade, Kaczocha, Studholme and Deutsch (2003) Proc. Natl. Acad. Sci. U.S.A. 100, 4269-4274]. In the present study, we show that FAAH alone cannot account for the facilitated diffusion of AEA across the cell membrane. In particular, (i) using a short incubation time (90 s) to avoid AEA hydrolysis by FAAH, AEA accumulation into rat basophilic **leukemia** or C6 cells was saturable at low μM concns. of substrate and non-saturable at higher concns.; (ii) time-dependent and, at low μM concns. of substrate, saturable AEA accumulation was observed also using mouse brain synaptosomes; (iii) using synaptosomes prepared from FAAH-deficient mice, saturable AEA accumulation was still observed, although with a lower efficacy; (iv) when 36 AEA and N-oleoylethanolamine analogs, most of which with Ph rings in the polar head group region, were tested as inhibitors of AEA cellular uptake, strict structural and stereochem. requirements were needed to observe significant inhibition, and in no case the inhibition of FAAH overlapped with the inhibition of AEA uptake; and (v) AEA biosynthesis by cells and sensory neurons was followed by AEA release, and this latter process, which cannot be facilitated by FAAH, was

still blocked by an inhibitor of AEA uptake. We suggest that at least one protein different from FAAH is required to facilitate AEA transport across the plasma membrane in a selective and bi-directional way.

CC 13-2 (Mammalian Biochemistry)

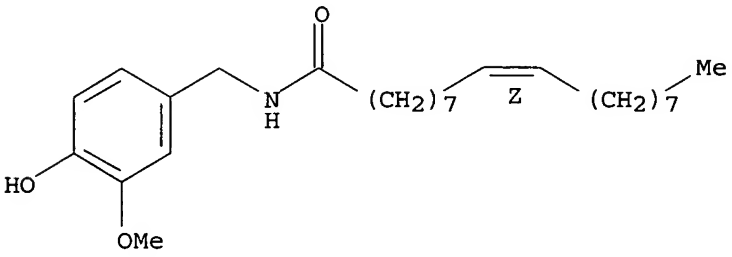
IT **58493-49-5** 108455-80-7 **128007-31-8** 135391-28-5
203849-07-4 203849-08-5 223593-61-1 616884-62-9 616884-63-0
616884-64-1 616884-65-2 709671-71-6 709671-74-9 709671-77-2
709671-80-7 709671-83-0 709671-86-3 709671-89-6 709671-92-1
709671-95-4 709671-98-7 709672-09-3 709672-12-8 709672-16-2
709672-19-5 709672-22-0 709672-24-2 709672-25-3 709672-26-4
709672-27-5 709672-28-6 709672-29-7 709672-30-0 709672-31-1
709672-32-2 709672-33-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(AEA analog, uptake; evidence for existence of specific fatty acid amide hydrolase-independent process for membrane transport of endocannabinoid anandamide (AEA))

IT **58493-49-5 128007-31-8**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(AEA analog, uptake; evidence for existence of specific fatty acid amide hydrolase-independent process for membrane transport of endocannabinoid anandamide (AEA))

RN 58493-49-5 HCAPLUS

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

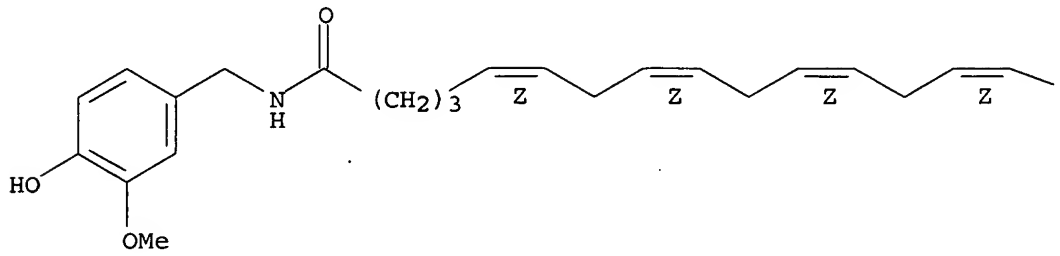


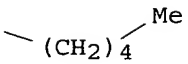
RN 128007-31-8 HCAPLUS

CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A





REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:203609 HCAPLUS
DOCUMENT NUMBER: 137:56979
TITLE: A structure/activity relationship study on arvanil, an endocannabinoid and vanilloid hybrid
AUTHOR(S): Di Marzo, Vincenzo; Griffin, Graeme; De Petrocellis, Luciano; Brandi, Ines; Bisogno, Tiziana; Williams, William; Grier, Mark C.; Kulasegram, Sanjitha; Mahadevan, Anu; Razdan, Raj K.; Martin, Billy R.
CORPORATE SOURCE: Endocannabinoid Research Group, Istituto di Chimica Biomolecolare, Naples, Italy
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 300(3), 984-991
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:56979

AB Arvanil, a structural "hybrid" between the endogenous cannabinoid CB1 receptor ligand anandamide and capsaicin, is a potent agonist for the capsaicin receptor VR1 (vanilloid receptor type 1), inhibits the anandamide membrane transporter (AMT), and induces cannabimimetic responses in mice. Novel arvanil derivs. prepared by N-methylation, replacement of the amide with urea and thiourea moieties, and manipulation of the vanillyl group were evaluated for their ability to bind/activate CB1 receptors, activate VR1 receptors, inhibit the AMT and fatty acid amide hydrolase (FAAH), and produce cannabimimetic effects in mice. The compds. did not stimulate the CB1 receptor. Methylation of the amide group decreased the activity at VR1, AMT, and FAAH. On the aromatic ring, the substitution of the 3-methoxy group with a chlorine atom or the lack of the 4-hydroxy group decreased the activity on VR1 and AMT, but not the affinity for CB1 receptors, and increased the capability to inhibit FAAH. The urea or thiourea analogs retained activity at VR1 and AMT but exhibited little affinity for CB1 receptors. The urea analog was a potent FAAH inhibitor (IC50 = 2.0 μM). A water-soluble analog of arvanil, O-2142, was as active on VR1, much less active on AMT and CB1, and more potent on FAAH. All compds. induced a response in the mouse "tetrad", particularly those with EC50 <10 nM on VR1. However, the most potent compound, N-N'-di-(3-chloro-4-hydroxy)benzyl-arachidonamide (O-2093, ED50 .apprx.0.04 mg/kg), did not activate VR1 or CB1 receptors. Our findings suggest that VR1 and/or as yet uncharacterized receptors produce cannabimimetic responses in mice in vivo.

CC 1-3 (Pharmacology)
Section cross-reference(s): 63

IT Amide group
Anti-inflammatory agents
Antitumor agents

Drug design
Hydroxyl group
Methoxy group
(structure/activity relationship study on arvanil)

IT **322399-59-7P**, O-1861 439079-98-8P, O 1988 439079-99-9P, O 1986
439080-00-9P, O 2094 439080-01-0P, O 2093 439080-02-1P, O 1987
439080-03-2P 439080-04-3P, O 2109 439080-05-4P, O 2142
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure/activity relationship study on arvanil)

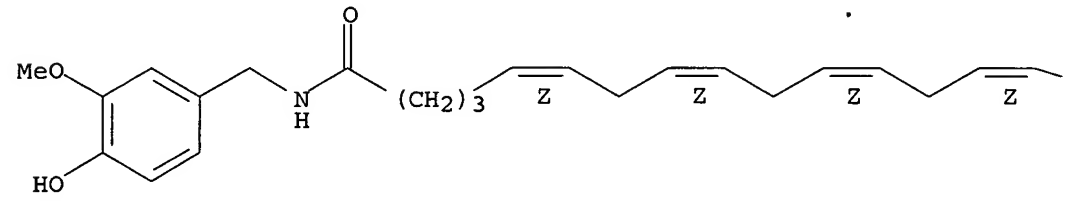
IT **128007-31-8P**, Arvanil
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(structure/activity relationship study on arvanil)

IT **322399-59-7P**, O-1861
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; PRP (Properties); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure/activity relationship study on arvanil)

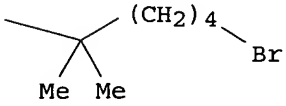
RN 322399-59-7 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, 20-bromo-N-[(4-hydroxy-3-methoxyphenyl)methyl]-16,16-dimethyl-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



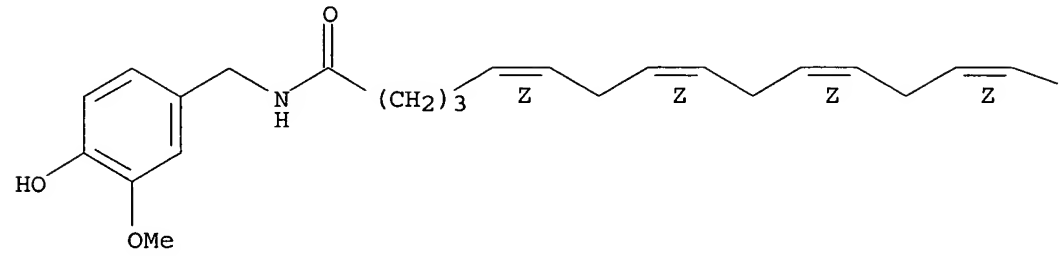
IT **128007-31-8P**, Arvanil
RL: **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; RCT (Reactant); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(structure/activity relationship study on arvanil)

RN 128007-31-8 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-,

(5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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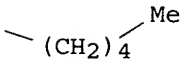


REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:272650 HCAPLUS
DOCUMENT NUMBER: 141:99178
TITLE: Effect of capsaicin and N-docosahexaenoyl-vanillylamide on growth of taxol-tolerant HeLa cells
AUTHOR(S): Jin, Yongfu; Ishihata, Kimie; Kajiyama, Shin-ichiro; Fukusaki, Ei-ichiro; Kobayashi, Akio; Baba, Naomichi; Tada, Mikiro; Takahata, Kyoya
CORPORATE SOURCE: Graduate School of Natural Science and Technology, Okayama University, Japan
SOURCE: Nippon Shokuhin Kagaku Gakkaishi (2002), 9(2), 50-53
CODEN: NSKGF4; ISSN: 1341-2094
PUBLISHER: Nippon Shokuhin Kagaku Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

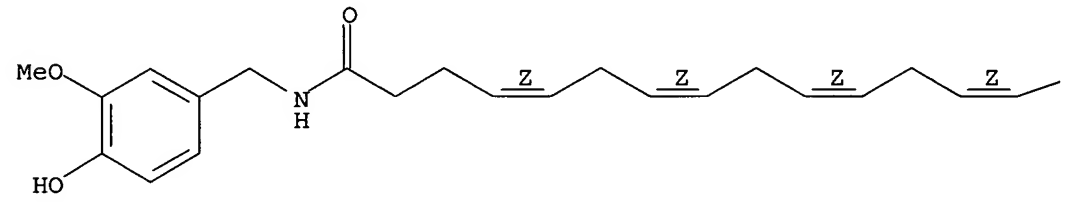
AB There are few effective clin. studies to inhibit the growth of multidrug resistance tumor cells. We have been interested in the physiol. actions of capsaicin (CAP), the pungent ingredient in hot chilli peppers, and polyunsatd. fatty acids, for example docosahexaenoic acid (DHA), extracted from fish oil. In this study, we synthesized a new vanillylamide derivative, N-docosahexaenoylvanillylamide (dohevanil), to investigate the inhibitory effect of dohevanil on growth of HeLa cells and taxol-tolerant HeLa cells. As a result, dohevanil has more potent inhibitory effect than CAP for both taxol-sensitive HeLa cells and taxol-tolerant HeLa cells. Particularly, the simultaneous addition of dohevanil and taxol more strongly induced cell death of taxol-tolerant HeLa cells. There results obtained in this study suggest that dohevanil has stronger inhibitory effect than CAP for the multidrug resistance cells.

CC 1-6 (Pharmacology)
IT **Antitumor agents**
Human

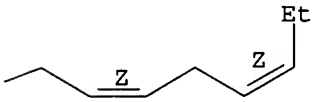
Multidrug resistance
(effect of capsaicin and N-docosahexaenoyl-vanillylamide on growth of taxol-tolerant HeLa cells)
IT 404-86-4, Capsaicin 33069-62-4, Taxol **571203-58-2**, Dohevanil
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effect of capsaicin and N-docosahexaenoyl-vanillylamide on growth of taxol-tolerant HeLa cells)
IT **571203-58-2**, Dohevanil
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(effect of capsaicin and N-docosahexaenoyl-vanillylamide on growth of taxol-tolerant HeLa cells)
RN 571203-58-2 HCAPLUS
CN 4,7,10,13,16,19-Docosahexaenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (4Z,7Z,10Z,13Z,16Z,19Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

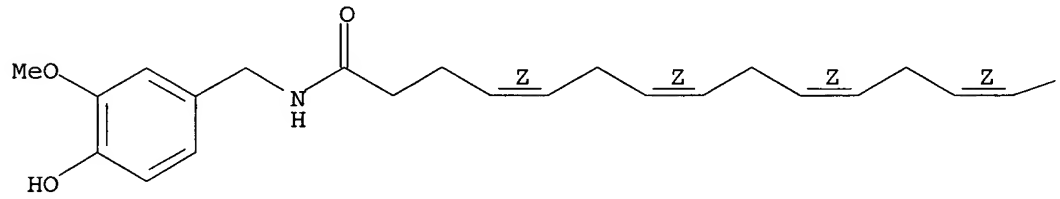


L40 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:937871 HCAPLUS
DOCUMENT NUMBER: 139:142982
TITLE: Induction of cancer cell apoptosis by docosahexaenoic acid (DHA) derivative Dohevanil of a spicy component capsaicin
AUTHOR(S): Takahata, Kyoya; Ishihata, Kimie; Kim, Eifuku
CORPORATE SOURCE: Department of Agriculture, Okayama University, Japan
SOURCE: New Food Industry (2002), 44(10), 6-12
CODEN: NYFIAM; ISSN: 0547-0277
PUBLISHER: Shokuhin Shizai Kenkyukai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. Induction of cancer cell apoptosis by docosahexaenoic acid (DHA) derivative Dohevanil of a spicy component capsaicin is reviewed including the structure of capsaicin and its receptor, antitumor effects of capsaicin as well as antitumor effects of Dohevanil.
CC 1-0 (Pharmacology)
IT **Antitumor agents**
Apoptosis
(induction of cancer cell apoptosis by DHA derivative Dohevanil, a spicy

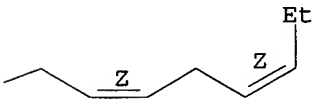
component capsaicin)
IT 404-86-4, Capsaicin 6217-54-5, Docosahexaenoic acid **571203-58-2**
, Dohevanil
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(induction of cancer cell apoptosis by DHA derivative Dohevanil, a spicy component capsaicin)
IT **571203-58-2**, Dohevanil
RL: **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(induction of cancer cell apoptosis by DHA derivative Dohevanil, a spicy component capsaicin)
RN 571203-58-2 HCAPLUS
CN 4,7,10,13,16,19-Docosahexaenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (4Z,7Z,10Z,13Z,16Z,19Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



L40 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:884754 HCAPLUS
DOCUMENT NUMBER: 136:161001
TITLE: Inhibition of rat C6 glioma cell proliferation by endogenous and synthetic cannabinoids. Relative involvement of cannabinoid and vanilloid receptors
AUTHOR(S): Jacobsson, Stig O. P.; Wallin, Thomas; Fowler, Christopher J.
CORPORATE SOURCE: Departments of Pharmacology and Clinical Neuroscience and Odontology, Umea University, Umea, Swed.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2001), 299(3), 951-959
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of the endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG) upon rat C6 glioma cell proliferation were examined and compared with a series of synthetic cannabinoids and related compds. Cells were treated with the compds. each day and cell proliferation was monitored for up to 5 days of exposure. AEA time- and

concentration-dependently inhibited C6 cell proliferation. After 4 days of treatment, AEA and 2-AG inhibited C6 cell proliferation with similar potencies (IC50 values of 1.6 and 1.8 μM, resp.), whereas palmitoylethanolamide showed no significant antiproliferative effects at concns. up to 10 μM. The antiproliferative effects of both AEA and 2-AG were blocked completely by a combination of antagonists at cannabinoid receptors (SR141716A and SR144528 or AM251 and AM630) and vanilloid receptors (capsazepine) as well as by α-tocopherol (0.1 and 10 μM), and reduced by calpeptin (10 μM) and fumonisin B1 (10 μM), but not by L-cycloserine (1 and 100 μM). CP 55,940, JW015, olvanil, and arachidonoyl-serotonin were all found to affect C6 glioma cell proliferation (IC50 values of 5.6, 3.2, 5.5, and 1.6 μM, resp.), but the inhibition could not be blocked by cannabinoid + vanilloid receptor antagonists. It is concluded that the antiproliferative effects of the endocannabinoids upon C6 cells are brought about by a mechanism involving combined activation of both vanilloid receptors and to a lesser extent cannabinoid receptors, and leading to oxidative stress and calpain activation. However, there is at present no obvious universal mechanism whereby plant-derived, synthetic, and endogenous cannabinoids affect cell viability and proliferation.

CC 1-6 (Pharmacology)
Section cross-reference(s): 2

IT **Antitumor agents**
(glioma; mechanism of the inhibition of rat C6 glioma cell proliferation by endogenous and synthetic cannabinoids)

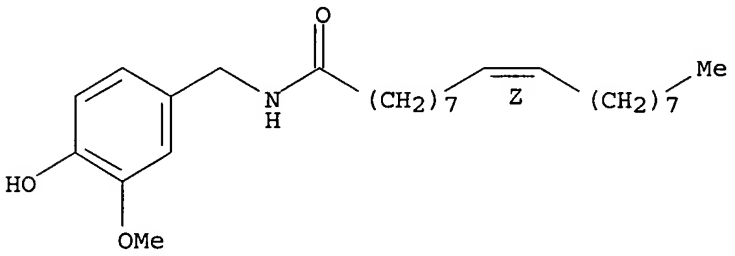
IT 404-86-4, Capsaicin 544-31-0, Palmitoylethanolamide 53847-30-6 **58493-49-5**, Olvanil 83002-04-4, CP55940 94421-68-8, Anandamide 131513-18-3, WIN55212 155471-08-2, JWH015 157182-49-5 187947-37-1
RL: BSU (Biological study, unclassified); **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(mechanism of the inhibition of rat C6 glioma cell proliferation by endogenous and synthetic cannabinoids)

IT **58493-49-5**, Olvanil
RL: BSU (Biological study, unclassified); **DMA (Drug mechanism of action)**; **PAC (Pharmacological activity)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(mechanism of the inhibition of rat C6 glioma cell proliferation by endogenous and synthetic cannabinoids)

RN 58493-49-5 HCAPLUS

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L40 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:209882 HCAPLUS
DOCUMENT NUMBER: 132:241970
TITLE: Pharmaceutical compositions containing N-acylvanillinamide derivatives capable of activating peripheral cannabinoid receptors
INVENTOR(S): Bisogno, Tiziana; Della Valle, Francesco; De Petrocellis, Luciano; Di Marzo, Vincenzo; Marcolongo, Gabriele; Melck, Dominique
PATENT ASSIGNEE(S): Innovet Italia S.r.l., Italy; Consiglio Nazionale Delle Ricerche
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000016756	A2	20000330	WO 1999-EP6980	19990921
WO 2000016756	A3	20000908		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IT 1302264	B1	20000905	IT 1998-MI2064	19980924
AU 9960860	A1	20000410	AU 1999-60860	19990921
EP 1115392	A2	20010718	EP 1999-947394	19990921
EP 1115392	B1	20021211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 229330	E	20021215	AT 1999-947394	19990921
ES 2189489	T3	20030701	ES 1999-947394	19990921
US 2005065216	A1	20050324	US 2004-949322	20040927

PRIORITY APPLN. INFO.:
IT 1998-MI2064 A 19980924
WO 1999-EP6980 W 19990921
US 2001-787764 B1 20010727

OTHER SOURCE(S): MARPAT 132:241970

AB Pharmaceutical compns. containing N-acylvanillinamide derivs. capable of activating the peripheral receptor CB1 of cannabinoids (Markush structures) are disclosed. N-(4-hydroxy-3-methoxybenzyl)oleyalmide (I) was prepared by the reaction of oleic acid, 4-methylmorpholine, and 4-hydroxy-3-methoxybenzylmine hydrochloride. The specific binding of I to mouse neuroblastoma cells and rat **leukemia** basophil cell was 1.64 μM and >15 μM, resp. A tablet contained 30, lactose 85, corn starch 75, talc 6, magnesium stearate 2, and CM-cellulose 2 mg.

IC ICM A61K031-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 25
IT **Antitumor agents**
(mammary gland carcinoma; pharmaceutical compns. containing N-acylvanillinamide derivs. capable of activating peripheral cannabinoid receptors)

IT **Antitumor agents**
(mammary gland; pharmaceutical compns. containing N-acylvanillinamide derivs. capable of activating peripheral cannabinoid receptors)

IT **Antitumor agents**
Mouthwashes
(pharmaceutical compns. containing N-acylvanillinamide derivs. capable of activating peripheral cannabinoid receptors)

IT **Antitumor agents**
(prostate carcinoma; pharmaceutical compns. containing N-acylvanillinamide derivs. capable of activating peripheral cannabinoid receptors)

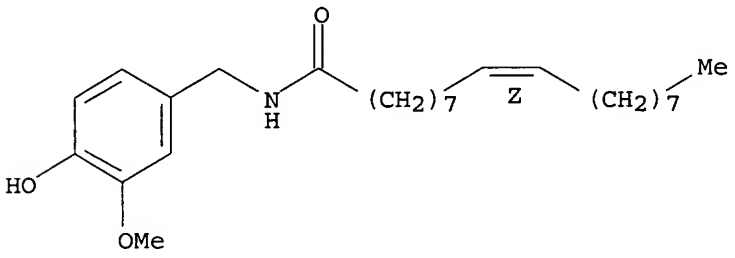
IT **Antitumor agents**
(prostate gland; pharmaceutical compns. containing N-acylvanillinamide derivs. capable of activating peripheral cannabinoid receptors)

IT **58493-49-5P 69693-13-6P 128007-31-8P**
261946-50-3P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. containing N-acylvanillinamide derivs. capable of activating peripheral cannabinoid receptors)

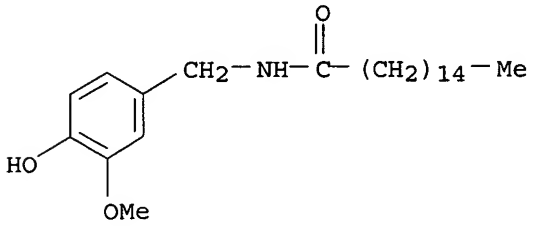
IT **58493-49-5P 69693-13-6P 128007-31-8P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. containing N-acylvanillinamide derivs. capable of activating peripheral cannabinoid receptors)

RN 58493-49-5 HCAPLUS
CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



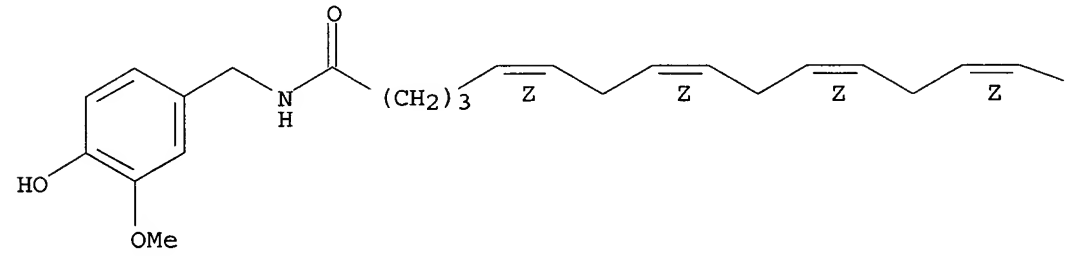
RN 69693-13-6 HCAPLUS
CN Hexadecanamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



RN 128007-31-8 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



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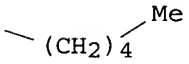


L40 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:4740 HCAPLUS
DOCUMENT NUMBER: 132:132746
TITLE: Suppression of nerve growth factor Trk receptors and prolactin receptors by endocannabinoids leads to inhibition of human breast and prostate cancer cell proliferation
AUTHOR(S): Melck, Dominique; De Petrocellis, Luciano; Orlando, Pierangelo; Bisogno, Tiziana; Laezza, Chiara; Bifulco, Maurizio; Di Marzo, Vincenzo
CORPORATE SOURCE: Istituto per la Chimica di Molecole di Interesse Biologico, Consiglio Nazionale delle Ricerche, Arco Felice, 80072, Italy
SOURCE: Endocrinology (2000), 141(1), 118-126
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Anandamide and 2-arachidonoylglycerol (2-AG), two endogenous ligands of the CB1 and CB2 cannabinoid receptor subtypes, inhibit the proliferation of PRL-responsive human breast cancer cells (HBCCs) through down-regulation of the long form of the PRL receptor (PRLr). Here the authors report that (1) anandamide and 2-AG inhibit the nerve growth factor (NGF)-induced proliferation of HBCCs through suppression of the levels of NGF Trk receptors; (2) inhibition of PRLr levels results in inhibition of the proliferation of other PRL-responsive cells, the prostate cancer DU-145 cell line; and (3) CB1-like cannabinoid receptors are expressed in HBCCs and DU-145 cells and mediate the inhibition of cell proliferation and Trk/PRLr expression. β-NGF-induced HBCC proliferation was potently inhibited (IC50 = 50-600 nM) by the synthetic cannabinoid HU-210, 2-AG, anandamide, and its metabolically stable

analogs, but not by the anandamide congener, palmitoylethanolamide, or the selective agonist of CB2 cannabinoid receptors, BML-190. The effect of anandamide was blocked by the CB1 receptor antagonist, SR141716A, but not by the CB2 receptor antagonist, SR144528. Anandamide and HU-210 exerted a strong inhibition of the levels of NGF Trk receptors as detected by Western immunoblotting; this effect was reversed by SR141716A. When induced by exogenous PRL, the proliferation of prostate DU-145 cells was potently inhibited (IC50 = 100-300 nM) by anandamide, 2-AG, and HU-210. Anandamide also down-regulated the levels of PRLr in DU-145 cells. SR141716A attenuated these two effects of anandamide. HBCCs and DU-145 cells were shown to contain (1) transcripts for CB1 and, to a lesser extent, CB2 cannabinoid receptors, (2) specific binding sites for [3H]SR141716A that could be displaced by anandamide, and (3) a CB1 receptor-immunoreactive protein. These findings suggest that endogenous cannabinoids and CB1 receptor agonists are potential neg. effectors of PRL- and NGF-induced biol. responses, at least in some cancer cells.

CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 14

IT **Antitumor agents**
Proliferation inhibition
(endocannabinoids suppression of NGF Trk receptors and prolactin receptors involvement in inhibition of human breast and prostate cancer cell proliferation)

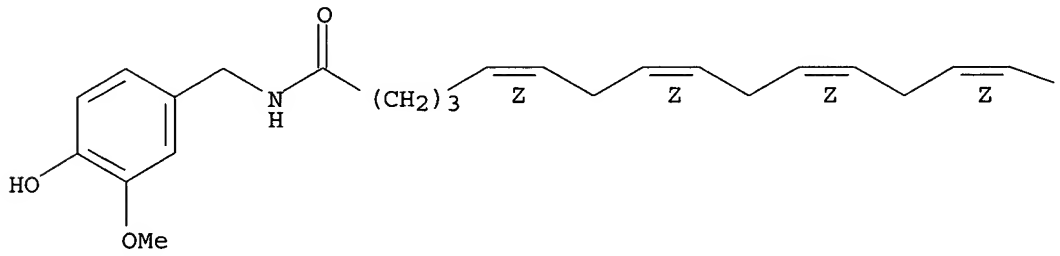
IT 53847-30-6 94421-68-8, Anandamide 112830-95-2, HU-210
128007-31-8, Arvanil 157182-49-5, (R)-Methanandamide
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(endocannabinoids suppression of NGF Trk receptors and prolactin receptors involvement in inhibition of human breast and prostate cancer cell proliferation)

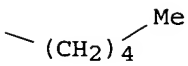
IT **128007-31-8**, Arvanil
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); BIOL (Biological study)
(endocannabinoids suppression of NGF Trk receptors and prolactin receptors involvement in inhibition of human breast and prostate cancer cell proliferation)

RN 128007-31-8 HCAPLUS
CN 5,8,11,14-Eicosatetraenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A





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L40 ANSWER 15 OF 16 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005039006 EMBASE
TITLE: Involvement of cannabinoids in cellular proliferation.
AUTHOR: Lopez-Rodriguez M.; Viso A.; Ortega-Gutierrez S.; Diaz-Laviada I.
CORPORATE SOURCE: M.L. Lopez-Rodriguez, Departamento de Quimica Organica I, Facultad de Ciencias Quimicas, Universidad Complutense, 28040 Madrid, Spain. mluzlr@quim.ucm.es
SOURCE: Mini-Reviews in Medicinal Chemistry, (2005) Vol. 5, No. 1, pp. 97-106.
Refs: 86
ISSN: 1389-5575 CODEN: MMCIAE
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050210
Last Updated on STN: 20050210

AB The endogenous canabinoid system (ECS) is involved in the regulation of an important number of central and peripheral physiological effects. Among all these functions, the control of the cellular proliferation has become a focus of major attention as opening new therapeutic possibilities for the use of cannabinoids as potential antitumor agents. The capacity of endogenous and synthetic cannabinoids to induce apoptosis of different tumoral cells in culture and in vivo, the mechanism underlying and the potential therapeutic applications are discussed in this review. .COPYRGT. 2005 Bentham Science Publishers Ltd.

CT Medical Descriptors:
*cell proliferation
*antineoplastic activity
regulatory mechanism
drug synthesis
apoptosis
cancer cell culture
in vivo study
drug mechanism
drug structure
mental disease: SI, side effect
mitosis inhibition
cell type
nerve cell
immunocompetent cell
endocrine cell

exocrine cell
experimental neoplasm: DT, drug therapy
human
nonhuman
short survey
Drug Descriptors:
*cannabinoid: AE, adverse drug reaction
*cannabinoid: AN, drug analysis
*cannabinoid: CM, drug comparison
*cannabinoid: DV, drug development
*cannabinoid: DT, drug therapy
*cannabinoid: EC, endogenous compound
*cannabinoid: PD, pharmacology
endocannabinoid: AE, adverse drug reaction
endocannabinoid: AN, drug analysis
endocannabinoid: CM, drug comparison
endocannabinoid: DV, drug development
endocannabinoid: DT, drug therapy
endocannabinoid: EC, endogenous compound
endocannabinoid: PD, pharmacology
dronabinol: AE, adverse drug reaction
dronabinol: AN, drug analysis
dronabinol: CM, drug comparison
dronabinol: DV, drug development
dronabinol: DT, drug therapy
dronabinol: EC, endogenous compound
dronabinol: PD, pharmacology
cannabidiol: AN, drug analysis
cannabidiol: CM, drug comparison
cannabidiol: DV, drug development
cannabidiol: EC, endogenous compound
cannabidiol: PD, pharmacology
cannabigerol: AN, drug analysis
cannabigerol: CM, drug comparison
cannabigerol: DV, drug development
cannabigerol: EC, endogenous compound
cannabigerol: PD, pharmacology
anandamide: AN, drug analysis
anandamide: DV, drug development
anandamide: DT, drug therapy
anandamide: EC, endogenous compound
anandamide: PD, pharmacology
2 arachidonoylglycerol: AN, drug analysis
2 arachidonoylglycerol: DV, drug development
2 arachidonoylglycerol: DT, drug therapy
2 arachidonoylglycerol: EC, endogenous compound
2 arachidonoylglycerol: PD, pharmacology
antineoplastic agent: AE, adverse drug reaction
antineoplastic agent: AN, drug analysis
antineoplastic agent: CM, drug comparison
antineoplastic agent: DV, drug development
antineoplastic agent: DT, drug therapy
antineoplastic agent: EC, endogenous compound
antineoplastic agent: PD, pharmacology
n acylethanolamine oleoylethanolamide: AN, drug analysis
n acylethanolamine oleoylethanolamide: DV, drug development
n acylethanolamine oleoylethanolamide: EC, endogenous compound
n acylethanolamine oleoylethanolamide: PD, pharmacology
2 methylarachidonyl 2' fluoroethylamide: AN, drug analysis

2 methylarachidonyl 2' fluoroethylamide: DV, drug development
2 methylarachidonyl 2' fluoroethylamide: PD, pharmacology
palmidrol: AN, drug analysis
palmidrol: CM, drug comparison
palmidrol: DV, drug development
palmidrol: EC, endogenous compound
palmidrol: PD, pharmacology
arvanil: AN, drug analysis
arvanil: DV, drug development
arvanil: EC, endogenous compound
arvanil: PD, pharmacology
olvanil: AN, drug analysis
olvanil: CM, drug comparison
olvanil: DV, drug development
olvanil: EC, endogenous compound
olvanil: PD, pharmacology
capsaicin: AN, drug analysis
capsaicin: CM, drug comparison
capsaicin: DV, drug development
capsaicin: EC, endogenous compound
capsaicin: PD, pharmacology
resiniferatoxin: AN, drug analysis
resiniferatoxin: CM, drug comparison
resiniferatoxin: DV, drug development
resiniferatoxin: EC, endogenous compound
resiniferatoxin: PD, pharmacology
dexanabinol: AN, drug analysis
dexanabinol: DV, drug development
dexanabinol: DT, drug therapy
dexanabinol: PD, pharmacology
cannabinoid receptor agonist: AN, drug analysis
cannabinoid receptor agonist: DV, drug development
cannabinoid receptor agonist: DT, drug therapy
cannabinoid receptor agonist: PD, pharmacology
jwh 133: AN, drug analysis
jwh 133: DV, drug development
jwh 133: PD, pharmacology
win 552122: AN, drug analysis
win 552122: DV, drug development
win 552122: DT, drug therapy
win 552122: PD, pharmacology
ucm 707: AN, drug analysis
ucm 707: DV, drug development
CT Drug Descriptors:
ucm 707: PD, pharmacology
omdm 1: AN, drug analysis
omdm 1: DV, drug development
omdm 1: PD, pharmacology
octadecanesulfonylfluoride: AN, drug analysis
octadecanesulfonylfluoride: DV, drug development
octadecanesulfonylfluoride: PD, pharmacology
2 methylarachinodyl 2' fluoroethylamide: AN, drug analysis
2 methylarachinodyl 2' fluoroethylamide: DV, drug development
2 methylarachinodyl 2' fluoroethylamide: DT, drug therapy
2 methylarachinodyl 2' fluoroethylamide: PD, pharmacology
ajulemic acid: AN, drug analysis
ajulemic acid: DV, drug development
ajulemic acid: PD, pharmacology
methanandamide: AN, drug analysis

methanandamide: DV, drug development
methanandamide: PD, pharmacology
2 methyl 3 (1 naphthoyl) 1 propylindole: AN, drug analysis
2 methyl 3 (1 naphthoyl) 1 propylindole: DV, drug development
2 methyl 3 (1 naphthoyl) 1 propylindole: DT, drug therapy
2 methyl 3 (1 naphthoyl) 1 propylindole: PD, pharmacology
4 (1,1 dimethylheptyl) 1',2',3',4',5',6' hexahydro 2,3' dihydroxy 6' (3 hydroxypropyl)biphenyl: AN, drug analysis
4 (1,1 dimethylheptyl) 1',2',3',4',5',6' hexahydro 2,3' dihydroxy 6' (3 hydroxypropyl)biphenyl: DV, drug development
4 (1,1 dimethylheptyl) 1',2',3',4',5',6' hexahydro 2,3' dihydroxy 6' (3 hydroxypropyl)biphenyl: PD, pharmacology
n (4 hydroxyphenyl)arachidonamide: AN, drug analysis
n (4 hydroxyphenyl)arachidonamide: DV, drug development
n (4 hydroxyphenyl)arachidonamide: PD, pharmacology
rimonabant: AN, drug analysis
rimonabant: DV, drug development
rimonabant: PD, pharmacology
unindexed drug
unclassified drug
hu 120
am 381

RN (dronabinol) 7663-50-5; (cannabidiol) 13956-29-1; (cannabigerol) 25654-31-3; (anandamide) 94421-68-8; (palmidrol) 544-31-0; (arvanil) **128007-31-8**; (olvanil) **58493-49-5**; (capsaicin) 404-86-4; (resiniferatoxin) 57444-62-9; (dexanabinol) 112924-45-5; (ajulemic acid) 137945-48-3; (methanandamide) 157182-49-5, 157182-50-8; (2 methyl 3 (1 naphthoyl) 1 propylindole) 155471-08-2; (4 (1,1 dimethylheptyl) 1',2',3',4',5',6' hexahydro 2,3' dihydroxy 6' (3 hydroxypropyl)biphenyl) 83003-12-7; (n (4 hydroxyphenyl)arachidonamide) 183718-77-6, 198022-70-7; (rimonabant) 158681-13-1, 168273-06-1

CN Hu 120; Jwh 133; Jwh 015; Cp 55940; Win 552122; Am 381; Ucm 707; Am 404; Sr 141716a

L40 ANSWER 16 OF 16 USPATFULL on STN

ACCESSION NUMBER:	2004:145171 USPATFULL
TITLE:	Anti-tumor pharmaceutical composition comprising N-vanillyl fatty acid amide
INVENTOR(S):	Takahata, Kyoya, Okayama-shi, JAPAN
PATENT ASSIGNEE(S):	KUREHA CHEMICAL INDUSTRY COMPANY, Limited (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004110844	A1	20040610	
APPLICATION INFO.:	US 2003-634641	A1	20030804	(10)

	NUMBER	DATE
PRIORITY INFORMATION:	JP 2002-353649	20021205

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	BOZICEVIC, FIELD & FRANCIS LLP, 200 MIDDLEFIELD RD, SUITE 200, MENLO PARK, CA, 94025
NUMBER OF CLAIMS:	14
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	6 Drawing Page(s)
LINE COUNT:	600

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides an anti-tumor pharmaceutical composition having a high anti-tumor effect with low side-effects.

The anti-tumor pharmaceutical composition comprises a N-vanillyl fatty acid amide of formula (1): ##STR1##

wherein --CO--R group represents a saturated or unsaturated fatty acid residue containing from 14 to 32 carbon atoms.

According to the invention, there was provided an anti-tumor pharmaceutical composition comprising a N-vanillyl fatty acid amide which relates to capsaicin wherein the composition has a low side-effect and a high anti-tumor effect, in particular an anti-**melanoma** effect and an anti-**leukemia** cell effect; and is very low pungent, stimulatory and preinflammatory effect.

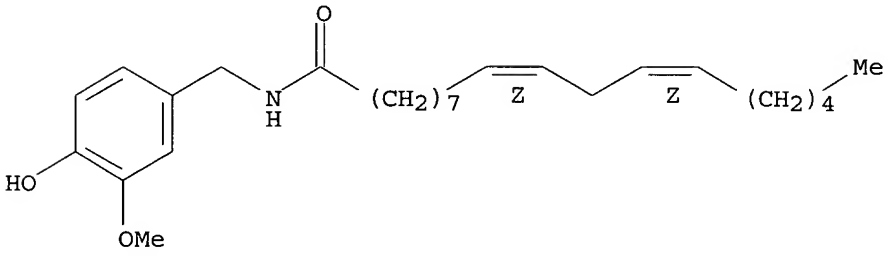
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT **16729-47-8P**, N-Vanillyllinoleamide **58493-49-5P**, N-Vanillyloleamide **69693-12-5P**, N-Vanillylmyristamide **104899-01-6P 457643-60-6P**, N-Vanillylricinoleamide **571203-58-2P**, Dohevanil **698373-40-9P** **698373-42-1P**
(preparation of antitumor vanillyl fatty acid amides)

RN 16729-47-8 USPATFULL

CN 9,12-Octadecadienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12Z)- (9CI) (CA INDEX NAME)

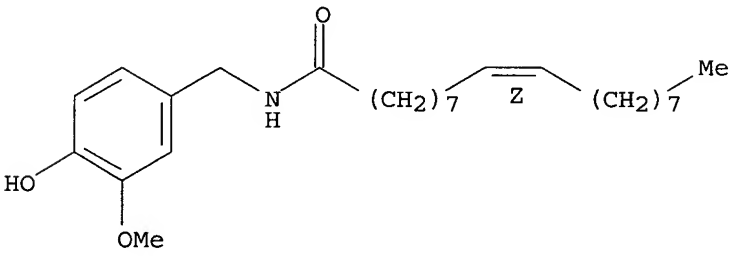
Double bond geometry as shown.



RN 58493-49-5 USPATFULL

CN 9-Octadecenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z)- (9CI) (CA INDEX NAME)

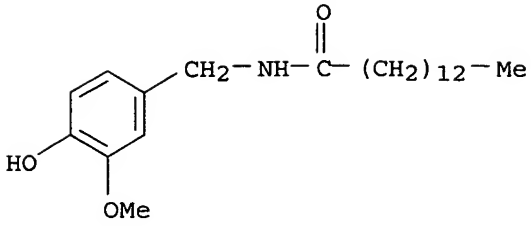
Double bond geometry as shown.



RN 69693-12-5 USPATFULL

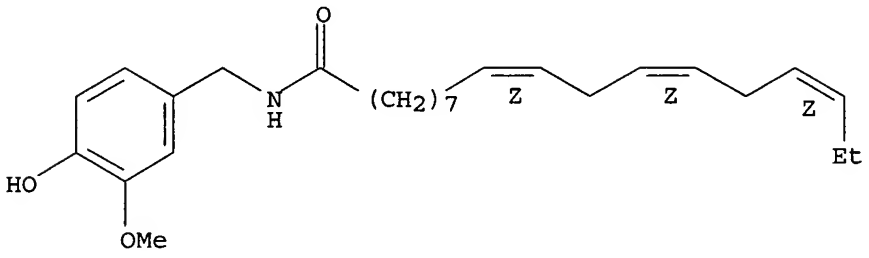
CN Tetradecanamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]- (9CI) (CA INDEX

NAME)



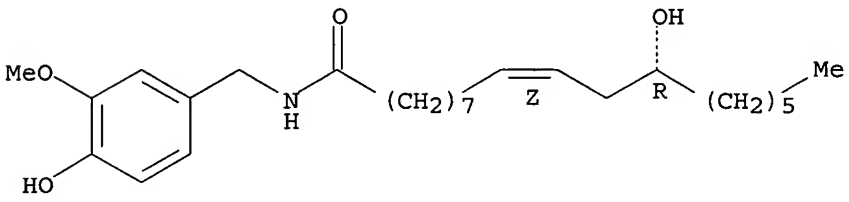
RN 104899-01-6 USPATFULL
CN 9,12,15-Octadecatrienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12Z,15Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 457643-60-6 USPATFULL
CN 9-Octadecenamide, 12-hydroxy-N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (9Z,12R)- (9CI) (CA INDEX NAME)

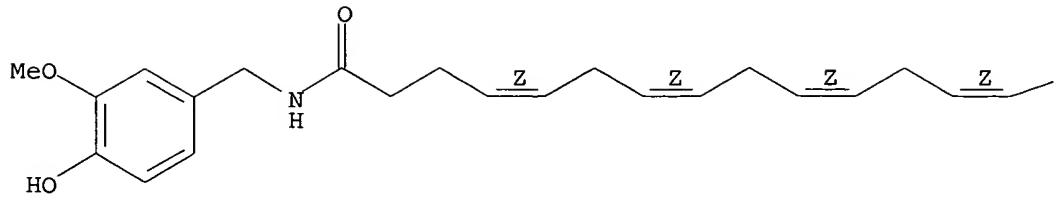
Absolute stereochemistry.
Double bond geometry as shown.



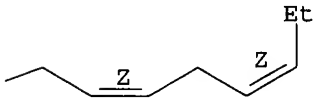
RN 571203-58-2 USPATFULL
CN 4,7,10,13,16,19-Docosahexaenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (4Z,7Z,10Z,13Z,16Z,19Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

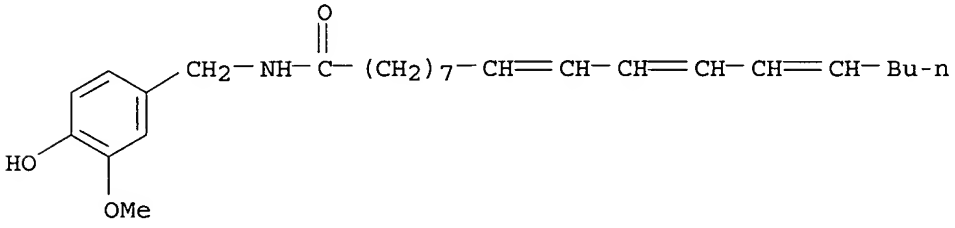
PAGE 1-A



PAGE 1-B



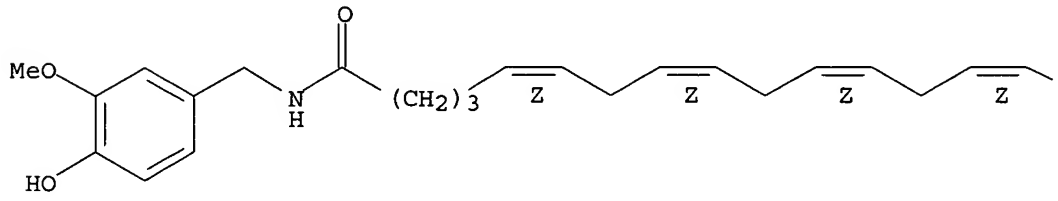
RN 698373-40-9 USPATFULL
CN 9,11,13-Octadecatrienamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



RN 698373-42-1 USPATFULL
CN 5,8,11,14,17-Eicosapentaenamide, N-[(4-hydroxy-3-methoxyphenyl)methyl]-, (5Z,8Z,11Z,14Z,17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B